Electrical stimulation in spinal cord injury

Smit, C.A.J.

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Development of a pressure ulcer prevention method

· Christof A.J. Smit ·

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Electrical stimulation in spinal cord injury

Development of a pressure ulcer prevention method

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Christophore Adrianus Johannus Smit

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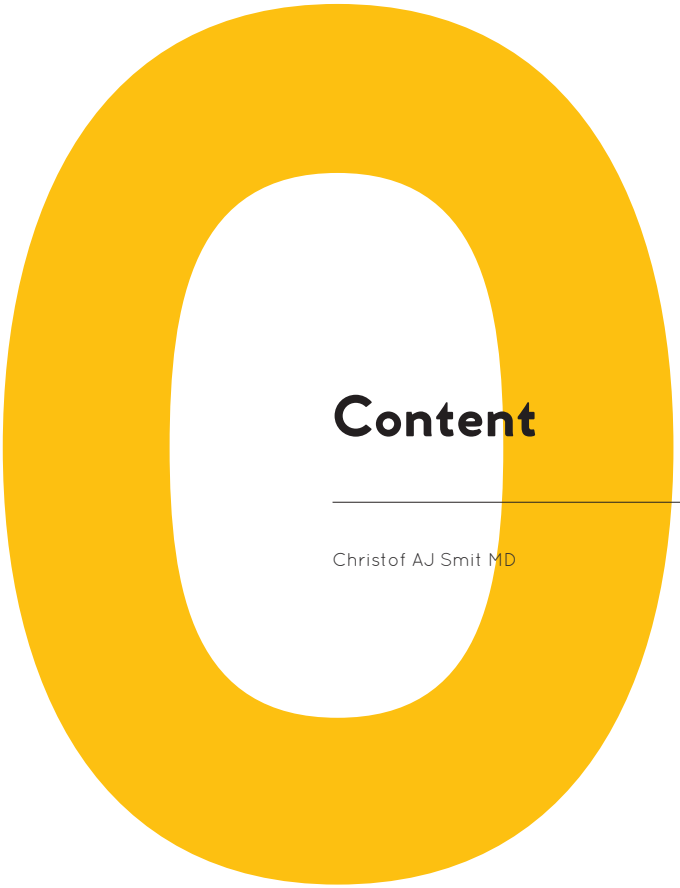
Promovendus:
drs. Christof A.J. Smit

Promotor:
prof. dr. Thomas W.J. Janssen

Copromotoren:
dr. Sonja de Groot
dr. Janneke M. Stolwijk-Swüste



Content

Christof AJ Smit MD

1

General introduction, objective and outline of the thesis

Christof AJ Smit MD

Background

Approximately 2.5 million people worldwide live with a spinal cord injury (SCI)[1]. SCI is a catastrophic event and causes the most drastic changes for an individual regarding physical status and lifestyle. These changes include impaired or absent motor control and sensibility below the level of the lesion, loss of normal bladder and bowel function, disturbed sexual function, and impaired autonomic nervous system[1]. Several studies have shown that SCI decreases the number of activities and participation (in society), and decreases the quality of life[1,3,48,66]. Before World War II, 80 % of people suffering from an SCI died within one year of the injury[1], with the main causes of death being pulmonary infections, infections in the urogenital system, and septicaemia caused by infections from pressure ulcers (PUs)[3]. Since the second half of the 20th century, there has been great progress in medical care and rehabilitation for individuals who have sustained an SCI, resulting in improvements in terms of life expectancy, functional capability and participation. However there is unfortunately still no treatment or cure for SCI, and SCI is to be considered a chronic condition[2,3]. The general population ages, and so do the people with an SCI[67]. The combination of the lack of cure, increased life expectancy and older age increase the number of secondary complications in people with an SCI.

Secondary complications after SCI

Several studies have reported that secondary complications after an SCI are very common. A study by Walter et al. in 2002 presents a list of self-reported secondary medical problems among 99 individuals with an SCI[65]. It shows high rates of current problems with pain (44 %) and PUs (38 %), next to respiratory (12 %) and bowel (14 %) problems. According to the 1998 National Spinal Cord Injury Statistical Center Annual Report[1,2], PUs are the most prevalent secondary complication in individuals with an SCI, and of individuals admitted to a Model Systems facility within 24 hours of SCI 34% developed at least one PU during acute care or rehabilitation. The prevalence in chronic SCI is unacceptably high, throughout their lives, up to 85%[1,2]. McKinley et al (1999), and others identified PUs as the most common secondary complication in all years after injury; and stated that an increased prevalence was associated with greater time since injury[41].

Pressure ulcers (PUs)

A PU is any lesion caused by unrelieved pressure resulting in damage of underlying tissue, involving the skin, fat, fascia, muscle, and bone. Therefore, unfortunately PUs are a common problem for wheelchair users such as individuals with SCI, as they are constantly sitting, unable to stand or walk. When a PU occurs it often does at bony prominences such as the ischial tuberosities, the trochanters or sacal region. Treatment can either be conservative or operative and very often consists of mandatory bed rest to release pressure of the wound(s) and of surgery, leading to radical consequences such as decreased mobility and independence,

Figure 1.
Examples of PU (at the buttocks) in two individuals with an SCI.
Photos published with permission.

delayed rehabilitation, and exclusion from work and social activities[3-5]. This has a tremendous effect on the individual's physical and psychological condition. The consequences (of the treatment, and mining revenues), also result in high costs for the community[1-4]. In figure 1 two people with an SCI and a PU (both at the buttocks, due to sitting) are shown.

Etiology of pressure ulcers

PUs develop following a prolonged period of compression of the tissue between a bony prominence, the skin and a surface, which causes the occlusion of capillaries and leads to tissue ischemia and necrosis[24,49,54,55,61]. Individuals with SCI are at increased risk for PUs due to factors such as reduced mobility, inability to adequately release pressure (e.g., standing up), atrophy of the paralysed muscles, a disturbed muscle pump function, reduced microcirculation, and impaired sympathetic function[20].

Inactive paretic muscles over time become stiff resulting in greater vulnerability[6,7,8]. In addition, due to an impaired sensation and the resulting hypo- or anesthesia of the sacral dermatomes, individuals with an SCI do not feel discomfort or pain and are often not aware of the necessity to relieve pressure. Paradoxically, the restoration of blood flow, vital to preserving tissue viability, has also been identified to cause extended damage of the tissue[22,43,58]. In instances where the ischemic state has been maintained for extended periods, the influx of oxygen-rich blood causes the activation of free radicals, further damaging the cells in the tissue[22,24,58]. In addition to the injury caused by biochemical changes occurring during tissue ischemia and ensuing reperfusion, high stress levels at the bone-muscle interface and the duration of their application have also been reported as direct causes of tissue injury[7,8,11,37-39]. Furthermore, injury to the muscle results in the formation of scar tissue, thus creating more foci for increased stress and leading to injury of adjacent previously healthy tissue[18,38].

It is the combined effect of pressure and or shear forces and these internal processes that cause the edema, inflammation, and necrosis that ultimately lead to formation of a PU[14,19,20,58,59]. PUs can be initiated at the dermis, usually in the presence of excessive friction and/or compromised dermal integrity and progress toward the deeper layers of tissue. Muscle is considered to be more susceptible to tissue degradation from mechanical loading and oxygen deprivation than dermis[7,31]; consequently, injury can also be induced in the deep tissue and progress outward[11], evolving into a severe full-thickness PU.
Presently, PUs are detected by visual inspection of the skin[46], often masking existing extensive damage to deeper tissue[11].

Current PU preventive measures are insufficient

In general, all individuals with an SCI should be considered at high risk for PUs due to risk factors, like muscle atrophy, loss of sensibility and reduced mobility, and should receive preventive strategies. Preventive measures are usually taken, and in daily clinical (medical) practice quite some effort is made to prevent PUs in individuals with an SCI, both by the multidisciplinairy rehabilitation teams and by the individuals themselves. A small list of measures taken or advised is listed in this paragraph. Prevention starts with the availability of custom-made wheelchairs and special pressure-relieving wheelchair cushions as well as special pressure relieving (air-) matrasses. Multidisciplinary rehabilitation teams advise on prevention by education, e.g. not to sit when having fever[2,3] and on healthy lifestyle in general, such as to avoid risk factors like smoking. Individuals with an SCI in rehabilitation programs learn how to perform adequate transfers (for example from bed to wheelchair and back), and to avoid skin or tissue damage due to shear forces. Furthermore, these individuals learn to perform pressure-relief movements while sitting in the wheelchair, like bending forward, to release pressure of the ischial tuberosities and restore compromised tissue and blood flow. Finally, individuals with an SCI in rehabilitation are taught to visually check skin condition twice every day, and when a PU occurs to immediately take adequate measures and consult a professional to prevent (further) tissue damage[2,3]. All mentioned measures reduce the risk of developing a PU, and need to be continued. These methods are all extrinsic methods (‘from outside the body’), trying to reduce pressure load, but unfortunately as mentioned above in the paragraph ‘secondary complications after SCI’, PUs still occur often, so these measures are (in many cases) insufficient.

New preventative interventions are needed

A problem with all the measures mentioned above is that they are passive measures that do not activate the muscles, which therefore do not ameliorate intrinsic risk factors (‘from inside the body’) for developing PUs such as muscle atrophy and decreased circulation[10, 15, 16]. Recognizing the absence of a significant reduction in the incidence of PUs,

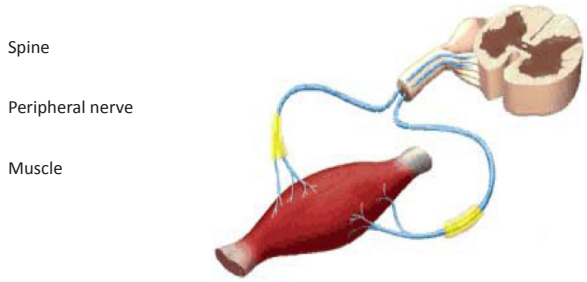


Figure 2.
Schematic picture of spine, nerve and muscle. Electrical stimulation can be applied to the nerve, consequently activating the muscle. The yellow areas indicate the peripheral nerve area where ES could be applied.

new preventative interventions are needed [32, 45, 54, 55, 59]. An active instead of passive way to prevent PUs and to increase tissue tolerance is to activate the paralysed muscles and increase tissue health. Healthy tissue, especially muscle tissue, is much better capable of tolerating deformation of cells and tissue due to pressure[4]. Active muscles stay healthy, and are less at risk to develop a PU[11,33]. Electrical stimulation (ES) can induce paralysed muscle contractions and thus activate the muscle. It can, therefore, possibly be an active method to prevent these wounds[36].

Electrical stimulation

The basic technique to induce muscle contractions for exercise via ES involves the use of an electrical stimulator providing impulses to skin surface (trans cutaneous) electrodes placed over the muscle to induce action potentials that would normally come from the central nervous system. These impulses in the motor neurons enter the muscle, subsequently activate the neuromuscular junctions to release acetylcholine. This will evoke action potentials in the entire motor unit (i.e. motor neuron and the skeletal muscle fibers it innervates), and hereby inducing muscle contractions. Thus, it is desirable to place the trans cutaneous electrodes directly over motor points (i.e., where the motor nerve enters the muscle) to obtain optimal muscle performance at relatively low ES current[21,24,48] (figure 2). Two other forms of applying ES are invasive techniques, i.e., intra-muscular stimulation with the use of implanted electrodes directly at the motor unit inside the muscle[46], and sacral anterior root (nerve) stimulation (SARS)[41]. It is theoretically possible that ES-induced muscle contractions can assist in PU risk reduction, since they have been shown to increase muscle mass, capillary density, as well as

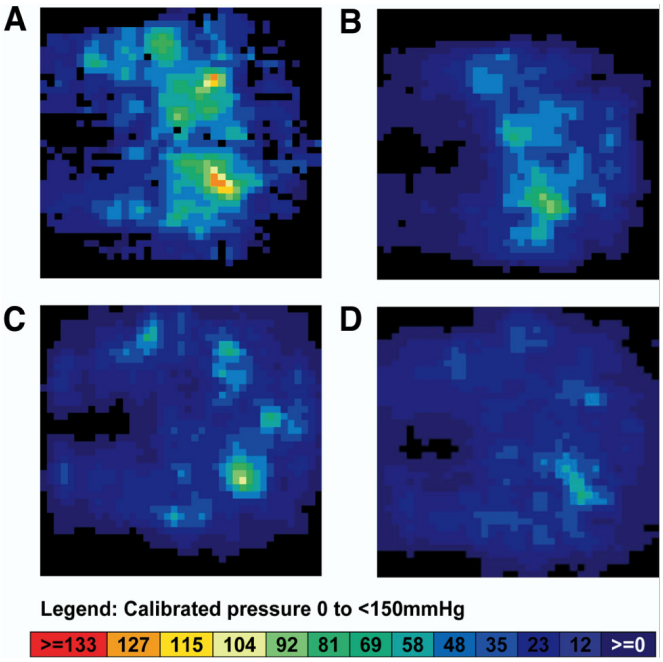


Figure 3.
Unprocessed pressure data maps for static mode seated pressure distribution in an individual with a SCI. Each image shows a representative interface pressure distribution at the cushion-subject interface (single frame from a 400-frame dataset). (A) Baseline, (B) initial daily use (post conditioning), (C) 6 months of daily use, and (D) 40 months of regular use. Images are orientated such that the thighs are toward to the left of the image and the right thigh toward the top. Each pixel corresponds to a calibrated interface pressure value (see legend).

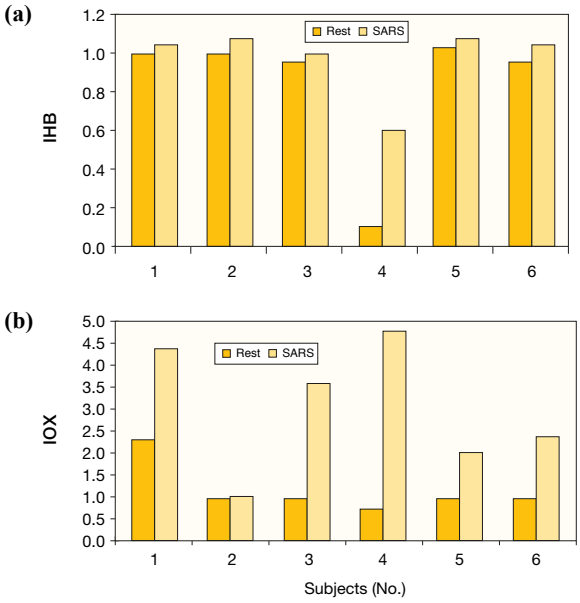


Figure 4. From Liu et al (2006)[41]
(a) Index of cutaneous hemoglobin (IHB) and (b) index of oxygenation (IOX) at rest and during ES (via sacral anterior root stimulator (SARS) implant) in six subjects with spinal cord injury.

skin and muscle blood flow[4,5,23,35-37,49]. We suggest that the acute mechanism of action of ES is twofold. Firstly, ES-induced contractions would 'reshape' the underlying muscle, thereby reducing the high stress levels experienced at the muscle-bone interface, lowering the amount of damage caused by the mechanical deformation and compression of the tissue[8,45].

Secondly, each contraction would also periodically restore blood flow and increase the oxygenation of the compressed tissue, reducing the amount of damage caused by long periods of ischemia and subsequent reperfusion[22,26]. In the longer term prolonged ES-induced muscle activation may increase muscle volume and induce structural improvement of pressure distribution, circulation and oxygenation. Numerous previous studies, that used a variety of ES-programs to recondition paralysed muscles, found that ES-induced muscle activation resulted in more volume, more strength and better circulation of the activated muscles[35-37, 49]. For example, Gerrits et al. (2002) found that 12 weeks of ES-induced paralysed muscle activation increased muscle volume and gave a significant increase in force of about 20%[19].

ES may be a useful intervention that helps to prevent complications like PUs and allows immobilized individuals to remain seated or supine for prolonged periods of time, reducing the necessary frequency of assisted repositioning, and, most importantly, reducing the

development of PUs. These periodically induced contractions may support or parallel the effects of passive methods like pressure-relief movements (voluntary or assisted repositioning), which are standard methods for PU prevention. In figure 3 and 4 effects of ES on respectively seating pressure, blood circulation and oxygenation in two studies[5,41] are shown.

Conceptual model for prevention of pressure ulcers

Pressure is the key factor in the development of PUs, and both intrinsic and extrinsic risk factors in- fluence tissue tolerance for deformity. A conceptual model for the development or etiology of PUs is presented in figure 5. This model pictures how primarily pressure causes a PU to occur[14,20,22,27].

The combination of intensity and duration of the pressure on soft tissue determines the total load of pressure on the soft tissue. Tissue tolerance for deformity determines if the total load of pressure is harmful, causing a PU to occur or not[45,52,54,58]. Tissue health and its tolerance for deformity therefore is important. Tissue health is influenced by several intrinsic and extrinsic factors. From the knowledge of the etiology of PUs as mentioned above we can identify in-

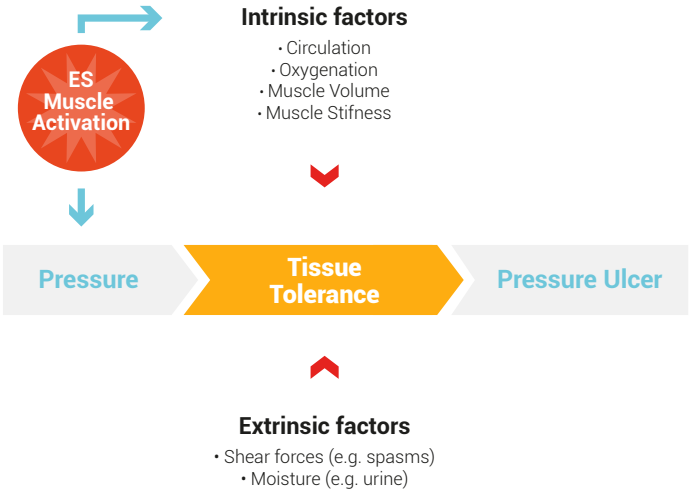


Figure 5.
Conceptual model of the etiology and prevention of pressure ulcers (PU's). Electrical stimulation (ES) increases tissue tolerance for deformity by reducing interface pressure and improving intrinsic factors

trinsic (from inside the body) factors such as circulation, oxygenation, muscle volume and/ or muscle stiffness[45,60,62], and extrinsic factors (from out- side the body), sheer forces and moisture (e.g.: transpiration, urine or feces)[60,67,68].
ES-induced muscle contractions could be helpful in increasing tissue tolerance. ES-induced muscle contractions could theoretically reduce (interface) peak pressure, and improve intrinsic factors, like muscle volume and circulation. The model shows how ES (the blue arrows) has effect on (interface) pressure, and on intrinsic factors, but no effect on the extrinsic factors. This could possibly be an active, instead of passive manner to reduce risk factors for developing PUs, and could be used in addition to the above-mentioned passive methods.

Development of a new PU prevention method

In recent years there has been an increased awareness of the need for physical exercise in this population, since has been demonstrated that they suffer more from inactivity related complications than the general population does[50]. Incorporated in some (but certainly not all) of the rehabilitation programs for SCI in the Netherlands is functional ES like leg cycling exercise (FES-LCE; or also 'Berkelbike'). This is an good and effective way to exercise and activate paralysed muscles. FES-LCE exercise though is not
practical for everyday use, and unfortunately this method cannot be used for prolonged periods of time or overnight, and will therefore have only limited acute and long term effects. Furthermore it does not have a (known) pressure relieving effect on the ischial tuberosities (buttocks). Besides, ES is used as an exercise (or even sport-) method, but not as an active way to prevent PUs. There is, as far as we know, no existing method to apply ES with the objective to prevent PUs. In figure 6 several current ES-methods are shown.

Figure 6.
ES-methods. b) FES- Leg Cycling exercise (LCE) using loose electrodes for transcutaneous ES

Physicians and therapists to date often seem not familiar with treatment options like ES. Both practical use of ES, and research in the field of PU prevention in SCI is difficult. There are limited scientific data available of each specific type of ES device. There are unanswered questions for example regarding the best ES protocol, optimal ES dose – response, what muscles to activate, and for how long before these muscles will stop contracting due to fatigue, and many more questions. Therefore, ES has long been a largely unknown and poorly understood modality[4,5,35-37].The prevention of PUs in clinical practice is not surprisingly generally empirical, and seems often based on dogma and rhetoric, rather than on evi- dence-based results.
In this thesis we have focussed on developing a new method for daily use as well as overnight, with the scope on the feasibility and practical use of FES. We developed specially ES-shorts, with embedded elec- trodes inside, that have never been used in previous research.

Objective of the thesis

Objective of this thesis was to identify the updated evidence of effects of ES induced muscle activation and to investigate feasibility of a new PU prevention method. We used specially developed ES-shorts and evaluated different protocols of surface intermittent ES to gluteal and hamstrings muscles in wheelchair-bound people with a SCI, in an attempt to develop this method.

Research questions

ES-induced muscle contractions could have positive effects on risk factors for the formation of PUs, but several research questions on feasibility and developing a method of applying ES have to be answered to support further research (prevention studies) and the practical (daily) use of ES. Research questions are:

- Can paralysed muscles be activated without problems?
- Is it better to activate only gluteal or both gluteal and hamstrings muscles to achieve the best ischial tuberosities pressure relief in sitting individuals with an SCI?
- Which of two stimulation protocols gives better results?
- Are the specially developed ES-shorts with the wires and the electro stimulator a feasible system? Is the ES system feasible for overnight use?

Outline of the thesis

Chapter 2 gives a literature overview of studies that investigate effects of ES on risk factors for developing PUs in persons with an SCI. All possible risk factors as well as their interrelations in literature are studied Although several risk factors are already mentioned in chapter 1 ('general introduction') and introduced in the conceptual model (page 13), they are here and described in more detail. This chapter helps to answer research questions.

Chapter 3 presents a pilot study (randomised clinical trial), in which we have studied the effects of surface ES of the gluteal muscles on the interface pressure. Only the gluteal muscle were activated. We wondered whether positive effects on the interface pressure would increase if more and larger muscles were activated, besides the gluteal muscles only.
Therefore in chapter 4 case control series are presented that compare the effects of electrically-induced activation of gluteal and hamstring muscles versus gluteal muscles only on sitting pressure distribution in individuals with an SCI. The usability of the newly developed ES-shorts used, is evaluated.
In chapter 5 the effects of on-off two duty cycles (protocol 1:1 versus 1:4 sec.) are studied during 3 hours of ES-induced gluteal and hamstring activation on interface pressure distribution in ten sitting individuals with an SCI, and the usability of the newly (and further) developed ES-shorts are investigated again.
We found no extensive literature describing the effect of ES on ischial oxygenation. Therefore in a pre and post intervention cohort 12 participants performed pressure-relief movements (PRM's) (like bending forward while sitting in the wheelchair), and then after finishing the PRM's in succession received surface ES to the gluteal and hamstring muscles while sitting in their own wheelchair. Therefore chapter 6 compares acute effects of ES-induced gluteal and hamstring muscle activation with pressure relief movements on interface pressure, blood flow and oxygenation.
In chapter 7 the feasibility of ES induced leg muscle activation was studied: muscle fatigue, sleep quality, and the usability of ES-shorts, during prolonged overnight use in people with an SCI. The ES-shorts have not yet been tested for extended stimulation protocols, lasting longer than 3 hours, and only acute effects have been studied.
The general discussion in chapter 8 reflects on the main findings and discusses the clinical implications. Finally the study design and limitations of the study and future perspectives are considered.

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2

Effects of electrical stimulation on risk factors for developing pressure ulcers in people with a spinal cord injury: a focused review of literature

Christof AJ Smit MD[1], Sonja de Groot PhD [1,2],
Janneke M Stolwijk-Swuste MD, PhD[3],
Thomas WJ Janssen PhD[1,4]

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ABSTRACT

Pressure ulcers (PUs), are a common and serious problem for wheelchair users, such as individuals with spinal cord injury (SCI), resulting in great discomfort, loss of quality of life and significant medical care costs. Therefore, it is of utmost importance to prevent PUs. In this literature overview the effects of electrical stimulation (ES) on the risk factors for developing PUs in people with an SCI are examined and synthesized. from January 1980 to January 2015. Thirty-four relevant studies in terms of PU prevention in SCI were identified. Four were randomised clinical trials (RCT's), 24 were case series, six had other designs. Three types of ES modalities were identified. The methodological quality varied from poor to fairly strong, with a large variety in used ES parameters. Twenty-three studies were identified describing acute effects of ES on interface pressure, oxygenation and/or blood flow, and 24 studies described the chronic effects of ES on muscle volume, muscle strength and histology. While there is a lack of controlled studies on the effects of ES on PU incidence, which disallows definite conclusions, there is moderate evidence to suggest that ES-induced muscle activation has a positive influence on several risk factors for developing PUs in people with an SCI.

Introduction

Skin-related secondary disabilities, especially pressure ulcers (PUs), are a common problem for wheelchair users such as individuals with spinal cord injury (SCI) resulting in great discomfort and significant medical care costs[1,2,3]. All individuals with SCI, and particularly those with complete lesions, are considered to be at high risk of PU development throughout their lifetime[2,3]. According to the Model SCI System Statistical Center, approximately 15% of individuals with SCI will develop a PU within the

first year of injury and approximately 27% over the first 25-years period post injury[1]. Even up to 85% of adults with SCI will develop a PU at some point during their lifetime[4-6]. Additionally, 40-80% of those who develop a PU will have at least one recurrence[2,4]. PUs are also among the most troublesome complications as they interfere with activities of daily living, occupational duties, and rehabilitation programs. In severe cases, PUs may even be life threatening[2].

PUs typically emanate in areas of the body where prolonged pressure and shear forces are being exerted on soft tissue over bony prominences, such as the sacrum and the ischial tuberosities, inducing cell deformation, inhibiting blood and oxygen supply, and ultimately causing (deep) tissue ischemiaand necrosis[2-6]. In literature, several, both intrinsic and extrinsic risk factors have been associated with the etiology of PUs. In figure 1 (page 24) these risk factors are presented in a schematic model. Pressure is the key factor in the development of PUs, and skin breakdown often occurs when the tissue tolerance for deformation due to pressure and shear forces in the areas of the ischial tuberosities is exceeded[7]. Individuals with SCI are at increased risk for PUs due to factors such as reduced mobility (wheelchair bound, with an inability to stand up and/ or relieve pressure), reduced microcirculation, impaired sympathetic nervous system function, atrophy of the paralysed muscles, and an absent muscle

pump function. In addition, due to an impaired sensory system as a consequence of the SCI, these individuals are often not aware of 'sleeping muscles', or pain, due to sitting in the same position for too long, and hence are not aware of the necessity to relieve pressure. Although it has been shown that preventive measures like custom-made wheelchairs, pressure relieving mattresses, (wheelchair) cushions and performing pressure-relief movements[9,12] can disperse pressure and forces and reduce the incidence of PUs, not all PUs are prevented and these wounds still often occur[1-7].

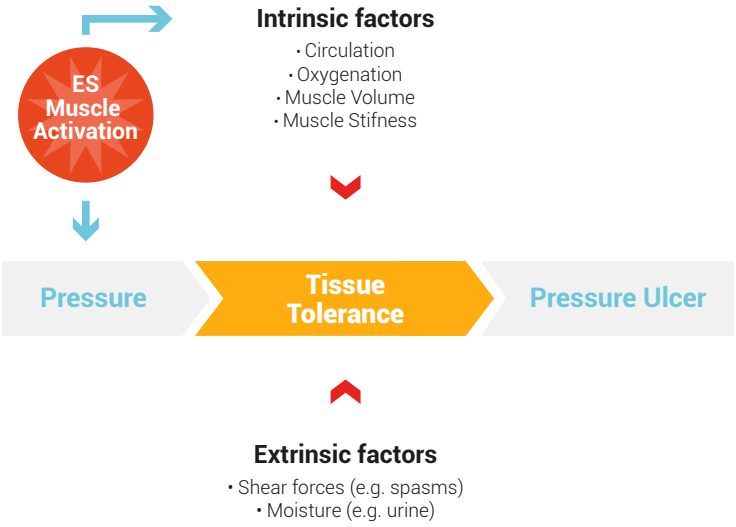

Figure 1.
A conceptual model for the occurrence of a pressure ulcer (PU) in SCI

It is theoretically possible, as can be seen in figure 1, that electrical stimulation (ES-) induced muscle activation can assist in PU risk reduction. ES-induced activation of paralysed muscles could possibly reduce peak sitting pressure and positively influence the intrinsic factors. In this way, ES could confer the benefit to PU care in SCI, as this could be an active, instead of passive, manner to reduce risk factors for developing PUs, and could possibly be used in addition to above-mentioned passive (no muscle activation) methods. However, to date, the clinical guidelines regarding the use of ES for PU management in SCI remain limited. This overview of literature was conducted to identify the present evidence, and to pinpoint the scope of the feasibility of future studis implementing ES for PU management in SCI.

Therefore, the objective of this literature overview is to describe:

- the used ES protocols and exercise modes in people with an SCI with preventive effects on the development of PUs;
- the effects of ES on PU risk factors in terms of prevention, as well as the cost-effectiveness of ES;
- recommendations for clinical (rehabilitation) practice, derived from (a number of) the selected studies.

Methods

Search method for identification of studies

To identify original articles on risk factors and/or preventive measures for PUs a full-text and keyword/ MESH terms search was performed using four databases (Medline, CINAHL, EMBASE, and the Cochrane Central Register of Controlled Trials), from January 1980 to January 2015.
Keywords for SCI (paraplegia, tetraplegia, spinal cord injury) and PUs (pressure ulcer, pressure sore, decubitus, ulceration and deep tissue injury) were combined with varying descriptions of keywords related to the development of PUs. These keywords were identified using broadly related search terms to wound prevention and treatment found in articles on this topic. We searched the literature, and by 'snowballing' we collected all the described keywords related to the development of PUs. This resulted in following words: (seating) pressure, shear force, sensibility, sensation, moisture, muscle volume, muscle stiffness, skin and/ or muscle atrophy, (blood) circulation, blood flow, (tissue) perfusion, and oxygenation.
We subsequently combined these words with any type of intervention using ES. Different terms for ES were: functional electrical stimulation (FES), transcutaneous or implant electrical (nerve) stimulation, neuromuscular electric stimulation (NMES), nerve root stimulation, and electrical therapy. Additional articles were located using the references cited in each of the articles retrieved by the electronic database search. Original studies were included in the review if they investigated ES as a muscle activation treatment modality, and therefore possibly indirectly as a PU-preventing measure.

Inclusion criteria

Articles published in English, German, French, or Dutch were included. All studies comparing ES with other methods were included without exclusion of any study design, except animal studies.

Methodological quality

For quality assessment, the Oxford quality scoring system ('Jadad-scale'), was used: a procedure to independently assess the methodological quality of a clinical trial. It is the most widely used assessment tool in reviewing, and as of 2008, its seminal paper has been cited in over 3000

scientific works (grade 1-4; 1= highest grade of evidence, 4 = lowest grade of evidence)[92]. For the non-clinical trials, the Downs & Black checklist was used, assessing the quality of original or primary source research articles and to synthesize evidence from quantitative studies (range 0-28 points; 0 = very poor, 28 very good quality)93. Case reports (n=4) were not assessed for methodological quality, as a single case report can be considered of poor quality (score: 4 on the Oxford quality scoring system) in comparison with any other type of study design reported in this overview of literature.

Outcome measures

Any outcome measure regarding the effectiveness of PU prevention was taken into account. The primary outcome measures of prevention criteria were:

- sitting (interface) pressure distribution;
- muscle oxygenation and blood perfusion;
- muscle size and volume;
- muscle histology and muscle fatigue.

Secondary outcome measures considered the potential difference between short and long term physiological effects of ES induced muscle activation, and the cost effectiveness of ES.

Results

Included studies

During the literature search, we identified a total of 165 unique references, of which the abstracts were further screened, subsequently generating 99 potentially relevant abstracts. The full texts of these 99 abstracts were retrieved and considered for eligibility for inclusion in this overview of literature, resulting in a total of 34 studies that met the inclusion criteria and were subjected to full-data extraction. Figure 2 provides a flow chart of the process and results for screening eligibility and study selection.

Thirty-four articles were included, 15 (44%) of which were conducted in the USA, 5 in the UK (15%), 4 in The Netherlands and in Australia (12%), 3 in Canada (9%), and the remaining 3 were from Denmark, Norway, and Austria. Of these 34 studies, 4 were RCT's (12%), one was a cohort study, and one a case-control study, 24 (71%) were case series, 4 were case reports (12%). The median number of participants was 12, with a range from 1 to 124.

Review of the studies (n=34)

Table 1 shows the quality classification of the selected studies. Three of the 34 studies were graded as providing strong evidence, in which the RCT scored > 3 according to the Oxford quality scale, in combination with adequate allocation concealment. Three studies provided fairly strong evidence (Grade 2), including one inadequately designed RCT and one cohort study. Twenty-four case series were classified as providing weaker evidence (Grade 3), and the

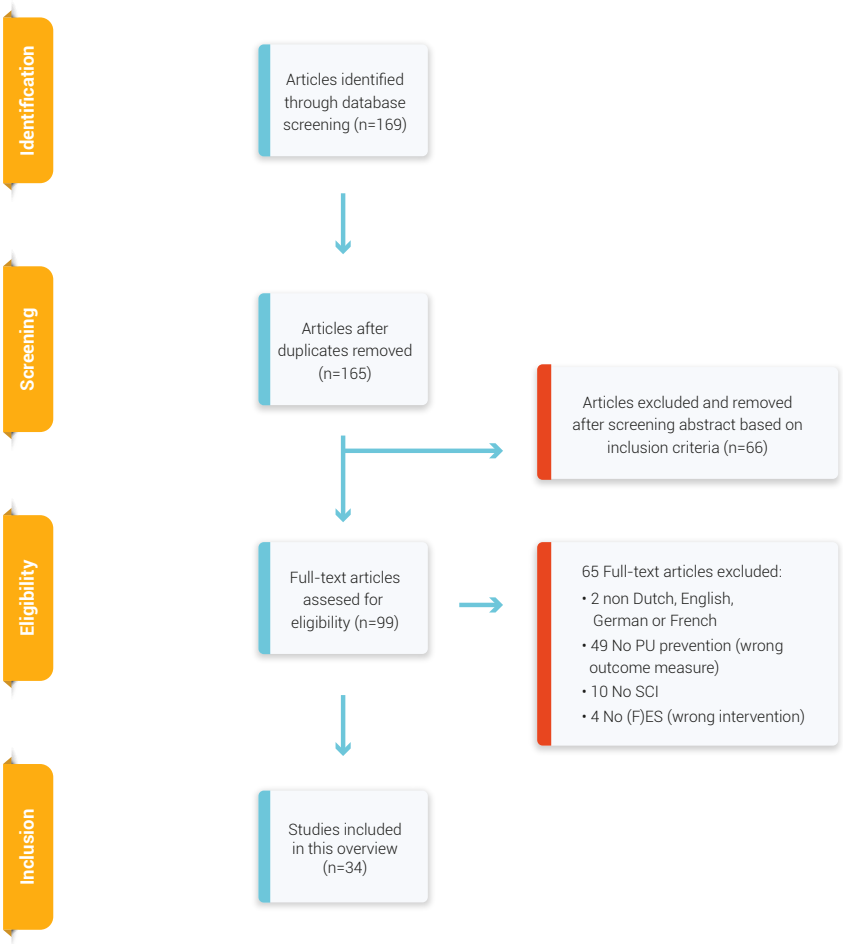

Figure 2.
A flow chart of the study selection process and results for screening eligibility and study selection

remaining four case reports were considered to demonstrate weak evidence only. In a total of 34 studies, only 4 were RCT's, with two of them being double blinded, and one having a cross-over design. In one of these studies the randomization process and sequence was clearly described. All four were of good methodological quality according to the Oxford quality scale score (Table 1).

Methodological quality on the Downs and Black tool was variable, from reasonably poor to good. Seven of the 30 trials scored 14 out of a total achievable score of 28, five scored 13, four scored 12, three scored 10, four had a score of 9, and three scored 8 (n=26). The results of all studies are described in the next paragraphs.

Intervention

Electrical Stimulation (ES).

Several of the selected articles pinpointed that the efficacy of ES is based on its protocols and parameters, such as the nature of the application technique, the stimulation frequency, intensity, and duration, as well as the number of times the muscle is stimulated in time (per hour, day or per week). Transcutaneous impulses are typically delivered at a frequency of 30-50 Hz to induce smooth, tetanic muscle contractions[8-10]. Sipski et al.(1993), Rodgers et al.(1991), Mohr et al. (1997), and Scott et al. (2003) reported that ES-induced exercise training, three times a week, twice a day for 30 minutes at a current amplitude of 4-30 mA,[28,29, 30,31,32] inducing tetanic contractions proved to be an optimal protocol regarding physiological effects of training, such as muscle volume and blood circulation.[29-35]

ES protocols and exercise modes

ES parameters and sites varied greatly across the selected studies: different stimulation frequencies, intensities, pulse duration, and waveform alongside diverse stimulating sites have been used. Overall, 20 studies used a frequency > 20 Hz, e.g. 25, 30, 40, 50 Hz, in order to induce tetanic muscle contractions; two other studies utilized low frequency of 10 Hz. The amplitude was in a range of 20–150 mA, while pulse duration ranged from 64 to 600 microseconds (μs).

The two most commonly described ES-induced exercise modes in the selected studies for individuals with an SCI are resistance exercise and endurance exercise[27-34]. Several studies have demonstrated that the same resistance training principles known to be effective for strengthening and inducing hypertrophy of the muscles of able-bodied individuals with voluntary exercise can be applied to ES-induced exercise of paralysed muscles[31-34]. These principles include isometric contractions, as well as dynamic concentric and eccentric contractions through a safe range of joint motion, progressive 'overload', several sets of exercise consisting of a relatively low number of repetitions at relatively high load resistance, and an exercise session frequency of 2-5 times per week[10-13]. Most research on ES-resistance exercise

Table 1
Characterstics of the included studies (n=34)

Study [ref]	Year published	Country	Sample size (n)	Design	Grade of evidencde (Oxford quality scale)
1. Bogie KM (12)	2006	USA	1	Case report	4
2. Liu LQ (13)	2006	UK	11	Case series	3
3. Ragnarsson KT (15)	1988	USA	30	Case series	3
4. Ragnarsson KT (25)	1988	USA	19	Case series	3
5. Petrofsky JS (16)	1984	USA	124	Cohort study	2
6. Pacy PJ (22)	1987	UK	4	Case series	3
7. Taylor PN (24)	1993	UK	20	Case series	2
8. Block JE (27)	1989	USA	3	Case series	3
9. Sipski ML (29)	1993	USA	28	Case series	3
10. Rodgers MM (30)	1991	USA	12	Case series	3
11. Mohr T (31)	1997	DK	10	Case series	3
12. Sloan KE (32)	1994	AUS	12	Case series	3
13. Chilibeck PD (34)	1999	CAN	6	Case series	3
14. Gerrits HL (35)	2001	NL	6	Case series	3
15. Ferguson AC (38)	1992	UK	9	Case series	3
16. Levine SP (39)	1990	USA	1	Case report	4
17. Smit CA (40)	2012	NL	10	Case series	3
18. Smit CA (83)	2013	NL	12	Case series	3
19. Dolbow DR (41)	2013	USA	8	Case series	3
20. Bremner LA (42)	1992	AUS	12	Case series	3
21. Rischbieth H (43)	1998	AUS	1	Case report	4
22. Hjeltnes N (44)	1997	N	5	Case series	3
23. Baldi JC (45)	1998	USA	1	Case report	4
24. Figoni SF (55)	1991	USA	14	Case series	3
25. Davis GM (58)	1990	AUS	6	Case control study	3
26. Olive JL (62)	2003	USA	9	RCT	1
27. Mawson AR (65)	1993	USA	32	Case series	3
28. Kainz A (67)	1988	A	?	Case series	3
29. Rochester L (70)	1995	UK	7	Case series	3
30. Martin TP (71)	1992	CAN	5	Case series	3
31. Londen A (82)	2008	NL	13	RCT	1
32. Wu GA (85)	2013	USA	7	Case series	3
33. Kim J (90)	2010	USA	6	RCT	1
34. Gyawali S (91)	2011	CAN	17	RCT	2

has been directed towards the paralysed quadriceps muscles due to their responsiveness to ES, proportional increase in force output with increasing ES current, and relative ease of exercise implementation. However, it is probable that this ES technique can be adapted to provide resistance exercise for other paralysed/weakened muscles as well.

For endurance exercise, a leg cycle ergometer (LCE) was developed in 1982, which is pedalled via ES- induced contractions of the paralysed lower-limb muscle groups[11,16,34,35]. Figure 3 illustrates operation of a commercially available ES-LCE by an individual with an SCI. Computer-controlled ES is used to induce contractions of the paralysed quadriceps, hamstring and gluteal muscle groups during proper angle ranges of the pedals to maintain smooth cycling. When pedalling at a 50-rates per minute (rpm) target rate, a total of 300 muscle contractions per minute are induced. To control the cyclic ES pattern and current intensity, a microprocessor that receives pedal position and velocity feedback information from sensors is incorporated. As muscle fatigue progresses during an exercise bout, ES current amplitude automatically increases to a maximum of about 140 m A to recruit non-fatigued muscle fibres in an attempt to maintain 50 rpm. When maximal current is reached and additional muscle fibre recruitment is no longer possible, the pedalling rate declines and ultimately falls below 35 rpm, at which time exercise is automatically terminated[34,35].

Figure 3.
ES-induced Leg Cycling Exercise by an individual with an SCI (published with permission)

Effects of ES on outcome measures

In total there were 23 of 34 studies that investigated acute effects of ES, 24 of 34 studies evaluated long- term effects and 13 measured both acute and long-term effects. Within the 23 studies that investigated acute effects, the outcome measures were either interface pressure or blood flow and oxygenation. Of the long-term effect studies, overall mean follow-up time was 12 weeks, with a range of 8 34 to 260 weeks (5 years)[12]. Outcome measures were interface pressure or incidence of PUs, and muscle volume or thickness, ischial tissue oxygenation, and sitting tolerance. In table 2 a-d, all studies on the effects of ES on the outcome measures (in SCI) are described, including the used ES-mode. In the next paragraphs these effects are described in more detail.

Acute effects

Interface pressure distribution

The results of ES on pressure distribution are shown in Table 1a (page 46). In all 34 of the selected studies, the authors stated that reducing prolonged mechanical loading at the skin as well as the muscle level may be critical in preventing PUs. The underlying mechanism of reducing pressure under the ischial tuberosities (while seated), during ES-induced muscle activation, has been suggested to be redistribution caused by either pelvic and/ or leg tilt, or changes of gluteal muscle force, tone or shape. We found no hard proof for this suggestion.

Several methods of applying ES were described in the articles. In figure 4 an electro stimulator with loose electrodes is shown. In five studies the gluteal muscles were activated [38,39,40,82,83], in one the quadriceps muscles while the lower legs were restrained[12]. In another three studies the effects of (F)ES cycling

Figure 4.
(example of) Neuro- pro (8-channel) electro stimulator

were studied[13,41,43]. All nine of the selected studies (n= 34), with grade of evidence 3 (n=6), 2 (n=2), and 1 (n=1), that have studied the dynamic acute effects of ES on interface pressure inducing ES-induced muscle contractions in SCI, indicate a moderate positive reducing effect on interface pressure[35-40].

Muscle oxygenation and blood perfusion.

Following an SCI, the interruption of spinal vasomotor pathways results in the loss of vasomotor control over skeletal muscle, skin, etc., which lowers the tone of the vascular bed below the level of the lesion. The impaired vascular patency causes the vessels to be less able to withstand normal loading conditions. Concurrent with the loss of capillary networks, and loss of muscle bulk, the volume of blood in the tissues is reduced. While microcirculation is crucial for tissue viability in terms of supply of oxygen and nutrients and removal of waste products, interrupted microcirculation leads to ischemia and local tissue starvation, which consequently leads to greater risk of PU formation[12,13,45]. Olive et al. (2003) in a RCT comparing able bodied (AB) with SCI individuals showed that regardless of muscle size, contraction rate or type of stimulation, blood flow significantly increased in activated muscles, in both AB and in SCI individuals[62.] The results of ES on muscle oxygenation and blood perfusion are shown in Table 1b (page 47).

Thirteen of 23 studies measured tissue oxygenation and/or blood flow, and 10 showed a significant increase of oxygenation and peak blood flow during ES, with 3 reporting inconsistent findings[55,62,65]. One of these three studied sub motor threshold muscle stimulation90. The two others (both level of evidence grade 3), studied acute effects of interface pressure, blood flow and/ or tissue oxygenation simultaneously [31,83].

Seven of 13 studies reported a significant increase of muscle and skin oxygenation[67,70]. Two case series (grade of evidence: 3) assessed the effects of a four and eight week period of exercise using ES in seven and eight participants, respectively. The reported mean of unloaded tissue oxygen levels increased post-exercise in both studies for 10 participants, but showed a decrease in 5 participants. The authors also indicated that there were no statistically significant differences between baseline and post-exercise tissue oxygen levels[41,70].

In summary, the methods and outcome measures varied in the studies, but the findings, although somewhat inconsistent, overall (10 of 13 studies) indicate positive changes in blood flow and/ or oxygenation due to ES-induced muscle activation.

Long-term effects

Muscle size and muscle volume

In table 1c (page 48) the results of ES on muscle size and volume are shown. There were 17 studies that explored the long-term effects of ES on muscle volume (and strength). Fifteen studies, incorporating progressive ES-induced muscle contractions especially using resistance exercise techniques, showed that atrophy of the paralysed muscles can be (partially) reversed[12,15, 27,29,32].

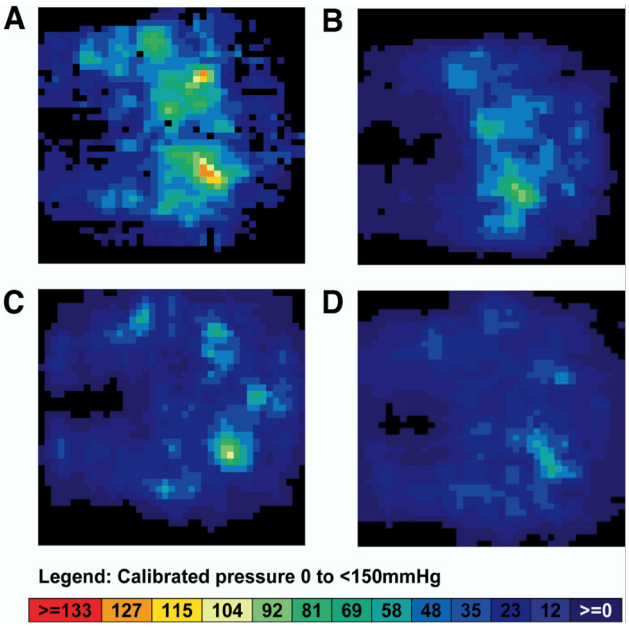

Figure 5.
Muscle hypertrophy after implanted gluteal stimulation system in a individual after 6 (C), and 40 months (D); (N=1). From: Bogie et al. APMR 2006 [12]

Several studies, of level 1 and 2 grade of evidence, showed that quadriceps muscle size returned to normal levels in individuals with SCI following ES training consisting of quadriceps muscle (knee extension) exercise[22-24]. One case report found a significant increase in muscle thickness after 5 years of muscle activation, using an implanted system for intra-muscular activation[12]. Similarly, ES-leg cycling exercise (LCE) training in individuals with SCI has been shown to elicit hypertrophy of the muscles employed as indicated by increased thigh circumference[16,25-29]. Moreover, the degree of muscle hypertrophy is most likely greater than indicated by circumference measurements since it has been shown that local adipose tissue (included in girth measurements) can be substantially reduced by ES-induced knee extension exercise[30] and ES-LCE[16]. Studies using the more sophisticated CT scan technique have confirmed significant increases in quadriceps area.[22,23,28,32,43] In figure 5 from Bogie et al (2006), the interface pressure of one individual with an implanted gluteal stimulation system is shown over a period of 40 months. Muscle hypertrophy occurred, reducing average interface pressure with 38 %12. Seven of 34 studies focused on the thigh area. Limited data (4 studies) are also available on a more relevant area for PU prevention in those with SCI, i.e. the gluteal region. Interesting results were found by Baldi et al.(1998), who used dual energy X-ray absorptiometry (DEXA) to

find that ES-LCE exercise training (figure 3), during the first 6 months post-injury could prevent the occurrence of gluteal muscle atrophy seen in a non-exercising control group. In figure 6 (from Baldi et al., 1998) is shown that this control group lost an average of 27% of gluteal lean mass during this period, whereas the ES-LCE group showed an increase of 5-10%[45].
Thus, concluding, ES-induced muscle activation, resistance and cycling exercise appear to have a marked effect on reversing the disuse atrophy of paralysed muscles, or retard the rate of its progression. Possibly, when started early after injury, ES-LCE could even be helpful in preventing muscle atrophy.

Muscle histology and muscle fatigue.
There were seven (of 34) studies that explored the long-term effects of ES on muscle There were seven (of 34) studies that explored the long-term effects of ES on muscle histology (n= 7), and/ or muscle stiffness (n= 2) and/ or fatigue (n= 5).
With regard to the effects on histology, results showed that the majority of muscle fibers were classified as type 2 pre- and post-training. Average fiber area and capillary number significantly increased with 23% and 39%, respectively, with ES-induced training[34]. Despite prolonged disuse, it is encouraging that resistance to fatigue and speed of contraction, together with oxidative capacity, rapidly revert towards normal values in response to daily treatments with ES at only twice motor threshold[70,71]. The period
of time following SCI does not appear to influence adversely the retraining of muscle properties by ES. The effects of training on strength and fiber type profile in paralysed muscles in individuals with an SCI, however, remain open and require further study. It is likely that the period of ES needs to be longer than 4 weeks and that the muscle stimulated should contract under load, if these parameters are to be significantly altered[70].
With regard to muscle fatigue, Scott et al. (2003) found that the use of ES to produce muscle contractions results in more rapid fatigue than comparable voluntary contractions. That is, loss in the force-generating ability of the muscle due to prior activation[33]. In addition, after SCI, paralysed muscles often become more easily fatigued, due to loss of both circulation and oxidative capacity due to a change from slow fatigue type 1 into fast fatigue type 2 muscle fibers[19,27,79]. Consequently, rapid fatigue has been one of the factors limiting the clinical effectiveness of ES.[28,30,40,79] Only few studies were found that described (long-term) training effects of ES-induced muscle activation, as can be seen in table 1d (page 49). Gerrits et al (2001) showed that that improved fatigue resistance of activated paralysed muscles (35 minutes of repeated quadriceps activation, 10-Hz trains 20s on, 50s off) was evident after only 2 weeks of stimulation. This rapid change in fatigue resistance seen in these ES-induced activated muscles suggests adaptations of mitochondrial function and possibly blood supply, which are known to respond rapidly to changes in muscle activity[35].
This paragraph showed several studies that reported that increased neuromuscular activity increases the oxidative capacity of the exercised muscles. ES of paralysed muscles increases

the proportion of type 1 fibers and can reverse the high susceptibility to fatigue of these muscles.

Adverse effects

In total, (only) four out of the selected 34 (preventive) studies reported on (potential) adverse events of ES. Among these four studies, two studies delivered ES using surface electrodes[29,30], while one study used a neuromuscular ES implant[12] and one used a sacral anterior root stimulation implant (SARS)[13].

All four of these studies reported no adverse events experienced by the participants in their study. The (potential) adverse effects described were skin problems using electrodes attached to the skin or technical problems with the implanted system.

Cost effectiveness

As mentioned in the introduction, PU`s are responsible for significant medical care costs[1,2,4,6]. In that respect we were interested in the PU prevention costs and cost effectiveness. Unfortunately we did not find a study in our search, determining (a model indicating) cost effectiveness of applying ES, or ES- induced exercise.

We therefore made our own calculation, and concluded that costs for using ES (i.e.: neuro stimulator with electrodes) are relatively low. The (loose) electrodes in figure 1 cost Euro 2.- (USD 2.70) each and can be re-used up to 3-4 times according to the manufacturer. For someone to use ES for 1 year 4 times per week once a day activating 2 muscle groups per leg would cost him approximately E 488.- (USD 679.-) per year. The neuro pro electro stimulator, more suitable for research objectives, shown in figure 2,

which lasts for 8-10 years, costs about E 1450 (USD 1972). The costs for commercial muscle stimulators are less (varying from E 200 (USD 272) to E 2400 (USD 2992)). The costs for hospital or rehabilitation center stay for treatment of PUs, more than E 1000 (USD 1360) per person per week, exceeds those costs by far: about E 400.000 (USD 544.000) per year[81].

We suggest a study model on preventive ES therapy including (i) health-related quality of life, (ii) patient satisfaction and global impression of change, (iii) healthcare resource utilization/ costs, and last but not least (iv) cost-effectiveness analysis. However, to study this, a large group of individuals with an SCI should be followed for several years, which is methodologically and logistically difficult. This is possibly one of the reasons that, to our knowledge, this study has not been done up till now.

Discussion

In the 34 studies selected in this overview a variety in several aspects was found, i.e. in outcome measure (acute and/or chronic) effects on interface pressure, blood flow, oxygenation, tissue adaptations like muscle strength and volume, tissue histology (and muscle fatigue) in stimulation parameters (resistance and endurance exercise), and in in ES modalities (applied currents, voltages, electrode placement and polarities varied between studies)[17-22]. Taken together the heterogeneity of study designs together with different outcome measures and ES modalities prevented us from performing a formal meta-analysis. It is hard to compare or combine results and even harder to draw definite conclusions. Nevertheless, as a whole, the 34 studies together suggested ES-enhanced reduction of risk factors for developing PUs.

Ten of 23 studies investigated the dynamic effect of ES and interface pressure, and all demonstrated beneficial effects. The quality of the studies varied from weak to moderate. In wheelchair users temporary seating-pressure reductions can be realized by regular pressure-relief movements, such as bending forward, actively performed by the user[83]. However, not all users are capable of performing these pressure-relief movements at all, or do not perform them on a regular basis hereby increasing the risk of prolonged mechanical loading. In this respect ES-induced muscle contractions are helpful, as the underlying mechanism of reducing pressure under the ischial tuberosities has been suggested to be pressure redistribution, caused by either a pelvic and/ or leg tilt, or changes in muscle form and tone[39,40]. ES-induced muscle contractions cannot replace the pressure-relief movements, but may be used additionally. ES-induced muscle activation is maybe not as effective in acute pressure relief, but the frequency of muscle activation stimulation is much higher than the performance of pressure relief movements, and could therefore be more effective in the long term.

ES-induced changes in circulation and oxygenation are most likely the result of the restoration of the sympathetic tone and vascular resistance below the level of the SCI, thereby increasing the perfusion pressure gradient in the capillary beds[65]. A dynamic pressure relief caused by gluteal muscle contraction and/or pelvic tilt, which dilates the micro vessels that underlie the ischial skin, may be involved[34].

Alternatively, increased blood perfusion may also have resulted from muscle contraction and allowed higher oxygen delivery rates and metabolite removal. Some of the selected studies[58,70,71] describe mechanisms of ES-induced increased blood flow, including a muscle pump effect, a cardiovascular response, and vasodilatation caused by local release of metabolites. Neuronal excitation and metabolic and cardiovascular responses may partially explain the increased blood perfusion[71]. The exact mechanism of the increased blood flow and oxygenation due to ES induced muscle contractions remains (somewhat) unclear, but it is well known that active muscles require more blood and oxygen than inactive or paralysed ones, and therefore are better perfused.

In 24 studies the long term-effect of functional ES in PU prevention in SCI was explored, and in 20 beneficial changes were reported, e.g., increased muscle volume, reduced interface pressure, increased tissue oxygenation, and interface (sitting) tolerance or a reduction of

the PU incidence after prolonged ES-induced muscle contractions. Four studies with non-significant findings all had relative shorter follow- up periods compared with the ones with positive (long term) findings, and are all grade 3 evidence.

However, among the studies with the positive findings on long term follow-up were two single case reports that provided the weakest evidence. All 24 studies mentioned muscular atrophy as one of the main factors that may contribute to the development of PUs in the longer term. This is especially the case among people with SCI, who often have severe atrophy of the muscles below the lesion level[13,26,40,49]. Counteracting this atrophy by ES-induced muscle contractions, increasing tissue tolerance for deformation, might, therefore, be a way to reduce PU incidence. Unfortunately, we found no studies describing the relation between time since injury and the effects of ES, nor studies describing risk or pre- cautions in the use of ES after many years since injury and muscle inactivity.

Regarding muscle stiffness there is an interesting study by Loerakker et al. (2013), which was not performed in SCI and is, therefore, not in the list of selected studies but it is worth mentioning. Loerakker et al. (2013) stated that it is essential to minimize internal muscle deformations in persons at risk of PUs. Individuals with SCI exhibit structural changes leading to a decrease in muscle thickness and stiffness, which subsequently increases the tissue deformations[46,47]. Muscle activity can reverse these effects, as muscle thickness and stiffness increases due to repetitive contraction and release, where cell properties to restrain stress forces improve[46,47]. These results indicate the importance of ES- induced muscle activity to decrease muscle stiffness, and restoring tissue properties after SCI, to prevent the development of PUs.

Two different types of (neuro muscular) ES have been identified in this overview, with the traditional surface or transcutaneous ES system being the most commonly used intervention with ES-shorts, as typical form of transcutaneous stimulation, and sacral anterior root stimulation (SARS). One of the more modern ways to use surface ES as described in the paragraph 'intervention' (above), is by hybrid cycling , using a tricycle with the propulsion coming from both arm and leg power. Arm power is voluntary while leg muscles are activated with ES, using ES shorts with embedded electrodes. Interestingly, one article on PU prevention reported ES as capable of stimulating gluteal muscles and hamstrings using a custom- made electrode garment with built-in electrodes (ES shorts)[40.] The ES shorts (Axiobionics, Ann Arbor, MI, USA) were custom-developed lycra shorts in which wires and surface electrodes were integrated. These were operated by placing two built-in surface electrodes over gluteal muscles and hamstring muscles on both sides. While this innovative device is easy to put on, and also avoids the need for skin preparation (thus overcoming some of the common disadvantages of traditional surface ES), the authors indicated that the key limitation of such a device is that the electrodes were fixed to one place in a one size of shorts[40]. Implanted ES systems include both SARS, utilizing electrodes implanted into the sacral S2, S3 and S4 nerve roots, and ES, with electrodes inside the muscle and either stimulators externally or implanted within the body. Several ES methods therefore are used, with advantages and disadvantages for each method.

Not described in the results of this overview, but worthwhile mentioning in this discussion

is the relationship between PUs and psychological and social factors and life adjustment after SCI. Psychological and social (behavioral) conditions associated with increased risk are aging and presence of co-morbidities, more years of smoking, the matrimonial status of the patient, belief in the susceptibility to pressure ulcers, and delay in seeking treatment or taking preventive measures[7,9,36,37]. ES-induced exercise has proven health benefits and improves overall quality of life. The collected research results also suggest that active training using ES might also have several therapeutic effects on psychological well-being of people with an SCI. A majority of the participants with an SCI indicated to have an improved self-esteem as a result of ES-induced training[29]. Therefore some effects as a result of physical inactivity and psychological problems after an SCI might be (partially) reversed by ES intervention.

Reviews or overviews of literature on a topic always present a number of limitations. These include publication bias (particularly against negative findings), language restrictions, and coding of key words. However, we performed a structured search, which was approved by a clinical librarian. A further limitation is the inclusion of case reports in the overview, which were classified as providing a low level of evidence. Nevertheless, these were studies presenting interesting findings and in our opinion contributed well to the aim and objectives of this overview to identify the updated evidence.

Discussing the clinical relevance, we wonder what conclusions should be drawn for clinical practice. Is it justified to conclude that based on the limited scientific evidence ES should not, or only on small scale, be used in clinical practice? We believe not. When taken together, the collectively efficacy studies and the collectively intervention studies provide a strong indication that ES has a direct positive effect on tissue and is, therefore, in all probability effective for PU incidence reduction. Furthermore, ES can be used in addition to (not instead of) regular preventive measures. Optimal positioning in a wheelchair, pressure reduction by cushions and regularly performing pressure-relief movements remain important in the prevention of PUs. Skin assessments should be incorporated into the patient's rehabilitation program, and overall daily comprehensive assessment. Overall, an active lifestyle should be advised, but besides that, this literature overview state the use of ES could be a part of that lifestyle. Additional work remains to be done to solve the problems associated with applying this technology in the clinical care and treatment of patients with an SCI.

Recommendations for clinical (rehabilitation) practice can be derived from a number of the selected studies, although it is hard to give a definite recommendation regarding the most adequate mode of ES, the optimal ES dose – response, training intensity, frequency or duration. Several studies (e.g.: Sipski et al. 1993, Rodgers et al.1991, Mohr et al. 1997 and Scott et al.2003) have reported that ES-induced exercise training, three times a week[29], twice a day[30,31] for 30 minutes at an intensity of 4-30 mA, inducing tetanic contractions proved to be a good, effective protocol regarding effects of training, like muscle volume and circulation[28,30,32]. Scott et al. (2003) also found that changing (altering) stimulation patterns during ES-induced exercise improves performance[33]. Participant's muscles contracted longer and stronger than when using the same stimulation pattern continuously. During a bout of exercise, the

muscle fibers undergo progressive fatigue and their force output decreases. To compensate for fatigue, ES current intensity must be progressively increased during the exercise bout to recruit fresh, non-fatigued muscle fibers, which is automatically accomplished in advanced electrical stimulator systems via performance feedback circuitry[9,34] .

It has long been established that preventing a PU occurrence is crucial for the SCI population and it is likely that both the low number of Grade 1 evidence, and the lack of practical guidelines has limited the implementation of ES for PU prevention. Future research is recommended to conduct more rigorous long-term clinical studies, as well as improve the design of ES devices and determine standardized outcome measures in prevention of PUs. Future work is therefore recommended and urgently needed in the form of well-designed clinical studies using large sample populations on determining the optimal stimulation location and parameters to confirm the beneficial effect on the enhancement of PU healing in SCI.

Conclusion

The used ES protocols and exercise modes in people with an SCI with preventive effects on the development of PUs are heterogeneous, making it difficult to compare results across studies. The methodological quality of the (PU prevention) studies included in this overview of literature was generally weak to moderate, as most of them were case series without control groups. Only a small number of studies that assessed the long-term effect of ES on PU risk factors (in terms of prevention), and firm conclusions or a definite statement on whether ES-induced exercise can actually prevent the incidence of PUs in SCI cannot be drawn. While there is a lack of controlled studies on the effects of ES on PU incidence, which disallows definite conclusions, there is moderate evidence to suggest that ES- induced muscle activation has a positive influence on several risk factors for developing PUs in people with an SCI: muscle atrophy can be (partially) reversed, skin and muscle blood flow can be augmented, and seating pressures can be reduced. It seems plausible that regular ES-induced exercise can reduce the PU incidence in people with an SCI. No (negative) side effects or complications of using ES in whatever manner or mode have been reported by participants of the studies. It is hard to give a definite recommendation regarding the most adequate mode of ES, the optimal ES dose – response, training intensity, frequency or duration. Nevertheless usable protocols have been described and can be used.

Clinical Message

- Based on available data there is moderate evidence that ES has short and long term positive influence on several risk factors for developing pressure ulcers: ischial tuberosities pressure, muscle volume, blood circulation, and tissue oxygenation in people with a spinal cord injury.
- ES is safe, relatively simple to apply, and costs are relatively low. There are several reasons to support the statement that ES should be considered more often in clinical practice for PU prevention in SCI.
- It is hard to give a definite recommendation regarding the most adequate mode of ES, the optimal ES dose – response, training intensity, frequency or duration. Nevertheless usable protocols have been described and can be used. For example: ES-induced exercise three times a week, twice a day, for 30 minutes at an intensity of 30 mA.

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Table 1 a-d

- Table 1a. Studies on the effect of ES on Interface Pressure.
- Table 1b. Studies on the effect of ES on muscle oxygenation & blood perfusion
- Table 1c. Studies on the effect of ES on muscle size, muscle volume & strength.
- Table 1d. Studies on the effect of ES on muscle histology, muscle stiffness & fatigue.

Abbreviations:
P, pulse; Freq, frequency; sec, seconds; ESLC, electrically stimulated leg cycling; HVPGS, high voltage pulsed galvanic stimulation; EMS, electrical muscle stimulation; NMES, neuro muscular electrical stimulation; IES, intermittent electrical stimulation; FES-LCE, functional electrical stimulation- leg cycling ergometry.
Continued part: SARS, sacral anterior root stimulation; BF, blood flow; FSA, force sensitive array; VO2 max, peak oxygen uptake; DEXA, Dual Energy X-ray absorptiometry.

Table 1a. Studies on the effect of ES on Interface Pressure			
Study	**Intervention & study size (number of participants, N)**	**Outcome**	**Effect**
Ferguson et al 1992 [52]	ES of quadriceps with restrained lower legs. N=9	Ischial tuberosities (IT pressure)	IT pressure signifiantly decreased (27-44 mmHg) ($p<0.05$).
Levine et al 1990 [53]	(acute) EMS of gluteal maximus. (N=?)	Tissue shape and deformation of gluteus maximus measured by echography	Redistributed internal pressure away from the bone ($p<0.05$). Consistent relationship between interface & intramuscular pressure.
Liu et al 2006 [65]	Stim freq of 20 pulses per sec; pulse width: 8-800 sec, amplitude: '1' for 10 sec. N=5	Ischial tuberosity pressure distribution (peak and distribution)	Significant reduction form 148.6 mmHg to 99.8 mmHg ($p<0.002$)
Dolbow et al2013 [69]	FES cycling 3 times per week. N=8	Interface pressure using force sensitive array (FSA).	Strong trend toward a reduction in average and maximal seat pressure ($p=0.052$)
Smit et l 2012 [70]	two 1-hour stimulation protocols. N=10	Interface pressure using force sensitive array (FSA).	Sign. IT Pressure reduction Best: both glutal and hamstrings muscles ($p=.01$).
Solis et al 2012 [73]	ES progressively applied to hind leg muscle. N=6	Relation between interface and internal pressure.	There is consistent relationship between external (interface) and internal (intramuscular) pressure.

Table 1b. Studies on the effect of ES on muscle size, muscle volume and strenght			
Study	**Intervention & study size (number of participants, N)**	**Outcome**	**Effect**
Pacy et al 1987 [13]	FES inducing aerobic of anaerobic exercise. N=4.	CT scan and histiology of vastus intermedius (activated muscles)	muscle increased 62.7% (p,0.01). Tendency of fibre type 1 increase from 7.0% to 26.0% (p<0.05).
Rodgers et al 1991 [21]	36 training sessions ES induced knee extension. N=12	Quadriceps muscle performance (strenght x repetitions)	Strenght of the quadriceps muscle and knee ROM significantly improved (p<0.05).
Rischbieth et al 1998 [25]	24 months of regular cyclic stimulation of the buttocks. N=1.	Muscle volume.	21% increase (p<0.05).
Hieltnes et al 1997 [26]	7 ES sessions per week for 8 weeks. N=5	Muscle volume (CT-scan)	Lean body mass sign. increased and muscles area increased from 267 (+/- 27) yp 324 (+/- 27) cm2 (p.0.05).
Baldi et al 1998 [27]	3-6 months ES-induced muscle contractioins. N= 26	Total body lean body mass; lower limb lean body mass; gluteal lean body mass (DEXA)	FES-CE, but not FES-IC training sigificantly causes muscle hypertrophy.
Boonyarom et al 2008 [62]	ES induced soleus muscle contractions in rats. Every other day for 2 wks. N> 10.	Muscle weight, number of muscle fibers type 1	Significantly suppresses muscle atrophy and retains muscle fiber proportions (P<0.05).
Dreibati et al 2010 [63]	ES-induced quadriceps contractions. 20 min sessions; 5 sec, 15 sec rest. N= 26.	Maximal voluntary quadriceps contraction	Higher intensity and higher frequency induce stronger contractions, but also stronger decline in force.
Bogie et al 2006 [64]	ES-induced contractions of the gluteal muscles daily, for more than 1 year. N= 1.	Gluteal muscle thickness.	Significant increase (p<0.05). [NM]ES became more effective as muscles strengthened over time.
Chou LW et al 2007 [66]	ES to isometric activate quadriceps muscle. N= 10.	Force-intensityrelationship.	Exponential significant relationship between muscle force and stimulation intensity.

Table 1c. Studies on the effect of ES on muscle histology, muscle stifness & fatigue			
Study	**Intervention & study size (number of participants, N)**	**Outcome**	**Effect**
Bajd et al 1989 [12]	ES on quadriceps and peroneus of 1 leg. N= 11.	Effect on tone and on spasticity	ES has tone and spasticity reducing effect.
Pacy et al 1987 [13]	ES-induced quadriceps muscle tarining, both aerobic and anaerobic. N= 4.	Effect on muscle volume, and histology.	Quadriceps muscle increased 62.7 % ($p<0.01$). Non significant histology, but tendency of fibre type 1 increase from 7- 26% ($p>0.05$).
Hieltnes et al 1997 [26]	ESLC 7 sessions per week for 8 weeks. N= 5.	VO2 max; muscle volume (DEXA and CT scan).	VO2 max increased 70% ($p<0.05$); lean body mass increased from 66.2 (+/-2.6) to 68.2 (+/- 2.1%) ($p<0.05$); muscles increased from 267 (+/- 27) to 324 (+/- 27) cm2.
Olive et al 2003 [40]	ES of the quadriceps muscles; work-rest cycle 1:6; 1:4 and 1:2 N= 17.	Blood flow femoral artery by Doppler ultrasound, and muscle fatigue (failure to contract).	Muscle fatigue was significantly greater (3-8 x ; $p<0.001$) in the SCI vs the able-bodied individuals.
Chilibeck et al 1999 [49]	FES-LCE 30 min, 3 days per week, 8 weeks. N= 6.	Muscle histiochemical characteristics; by biopsy	fibre area increased 23% ($p<0.05$), and capillary number increased 39% ($p<0.05$).
Boonyarom et al 2008 [62]	ES every other day for 2 wks in soleus muscle of rats; 20 vs 30 Hz. N > 20.	(soleus) muscle weight, number of muscle fibers type 1, based om histological properties	20 and 30 Hz significantly suppresses muscle atrophy and retains muscle fiber proportions ($P<0.05$).
Dreibati et al 2010 [63]	20 min sessions (or 60x) 5 sec ES of quadriceps, 15 sec rest. N= 26.	Maximal voluntary quadriceps contraction	Higher intensity and higher frequency induce significant stronger contractions, but also stronger decline in force $p<0.05$.
Scott et al 2003 [68]	Constant- and doublet-frequency FES trains of quadriceps. Doublets have a 5 msec rest- interval. N= 15.	Activation of the quadriceps muscle	Combining train types may be a useful strategy to offset rapid fatigue due to FES induced activation.

Table 1d. Studies on the effect of ES on muscle oxygenation & blood perfusion			
Study	**Intervention & study size (number of participants, N)**	**Outcome**	**Effect**
Hieltnes et al 1997 [26]	ESLC 7 sessions per week for 8 weeks. N= 5.	VO2 max; muscle volume (DEXA and CT scan).	VO2 max increased 70%; lean body mass increased with 6 % (and muscles increased; all significant p<0.05.
Kim et al 1995 [31]	Incremental one-legged dynamic knee extension exercise tests (40W) in able bodied. N= 6.	Muscle perfusion (Echo-doppler)	Significant increase p< 0.05.
Levine et al 1990 [32]	ES induced muscle activationin able bodied. N= 8.	Muscle (and tissue) perfusion using a radioactive tracer	Significant increase p< 0.05.
Janssen et al 2003 [39]	1-3 Hz twicth stimulation at 35 HZ in upper and lower leg muscles, inducing tetanic contractions. N= 12.	Blood flow Velocity measured by echo dopplerultrasonography	Significant increase (p<0.05) in the activated muscles
Olive et al 2003 [40]	ES of the quadriceps muscles; work-rest cycle 1:6; 1:4 and 1:2. N= 17	Blood flow femoral artery by Doppler ultrasound, and muscle fatigue (failure to contract).	Magnitude of the muscle blood flow to ES was not associated with increased muscle fatigue in SCI.
Scremin et al 1998 [41]	16 min of FES of quadriceps muscle. SCI versus able bodied control group. N= 10.	Muscle blood flow measured with positron emission tomography.	No (acute) differences between intervention and control group
Mawson et al 1993 [43]	High Voltage Pulsed Galvanic Stimulation (HVPGS); 3 experiments. 75 V, 10 Hz. N= 29.	Tissue oxygenation, measured by transcutaneous infrared spectoscopy.	Dose related increase of the perfusion pressure gradient in capillary beds of activated muscles up to 35 % (p<0.00001).
Gerrits et al 2001 [44]	Computer controlled FES- Leg Cycle Ergometer (FS-LCE). 6 weeks 3 times per week 30 min. N= 9.	arterial circulation using color coded duplex Doppler ultrasound.	Significant improvement of bloodflow to the lower limb. Resting diameter increased with 0.6 mm (+/- 1.5) (p<0.01).

3

The Effect of Surface Electric Stimulation of the Gluteal Muscles on the Interface Pressure in Seated People With Spinal Cord Injury

van Londen A, Herwegh M, van der Zee CH, Daffertshofer A, Smit CA, Niezen A, Janssen TW.

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ABSTRACT

The effect of surface electric stimulation of the gluteal muscles on the interface pressure in seated people with spinal cord injury. Arch Phys Med Rehabil 2008;89:1724-32.

Objective: To study effects of surface electric stimulation of the gluteal muscles on the interface pressure in seated persons with spinal cord injury (SCI).
Design: One session in which alternating and simultaneous surface electric stimulation protocols were applied in random order.
Setting: Research laboratory of a rehabilitation center.
Participants: Thirteen subjects with SCI.
Intervention: Surface electric stimulation of the gluteal muscles.
Main Outcome Measures: Interface pressure, maximum pressure, pressure spread, and pressure gradient for the stimulation measurement. Variables were compared using 2-tailed paired t tests.
Results: Alternating and simultaneous stimulation protocol caused a significant (P.01) decrease in interface pressure (–1712mmHg, –1914mmHg) and pressure gradient (–1211mmHg, –1412mmHg) during stimulation periods compared with rest periods. There was no significant difference in effects between the 2 protocols.
Conclusions: Surface electric stimulation of the gluteal muscles in persons with SCI causes a decrease in interface pressure. This might restore blood flow in compressed tissue and help prevent pressure ulcers.

Key Words: Decubitus ulcer; Pressure ulcer; Rehabilitation; Spinal cord injuries.

Pressure ulcers (PUs) are a common problem in people with a spinal cord injury (SCI).[1,2] They usually occur over bony prominences,[3] such as the ischial tuberosity, the major trochanter, and the sacrum. For people with SCI, pressure ulcers are a major problem because they limit mobility and independence and are an important cause of rehospitalization. Prevention of pressure ulcers is important for people with SCI to preserve mobility and independence and reduce health care costs.

People with SCI depend on wheelchairs for mobility and sit in a fixed posture for extended periods. This may result in long-lasting high pressure of the tissue over the bony prominences, which is a risk factor for developing pressure ulcers. Disuse atrophy of the paralysed muscles decreases the contact area with the support surface, whereas total pressure on the buttocks (ie, weight of the upper body) remains approximately the same, increasing local interface pressure even more. In addition, reduced blood flow below the level of the lesion contributes to the development of pressure ulcers. This reduction is caused by a loss of capillary network, failure of the skeletal muscle pump mechanism, muscle inactivity, drop in blood pressure, and occlusion of blood vessels.[4] These factors should be addressed in the prevention of pressure ulcers.

Several methods have been developed to prevent pressure ulcers by improving the interface

pressure distribution—for example, the use of different types of wheelchair cushions and the implementation of protective behavior (lifting, weight shifting, skin checks). Although the specially designed cushions may improve interface pressure distribution,[5] they do not reduce muscle atrophy. Protective behavior has no clear effect on the development of pressure ulcers,[6] and some actions may even be harmful—for example, lifting elicits high contact forces within the glenohumeral joint and requires a lot of muscle force,[7] possibly contributing to shoulder injuries. Apparently, these methods do not sufficiently meet the demands necessary for prevention of pressure ulcers. Hence, additional methods need to be studied.

Improvement in interface pressure distribution, reduction in muscle atrophy, and improvement in circulation are the uses of electric stimulation of the gluteal muscles.[8,9] Activating these muscles elicits a contraction, temporarily changing the shape of the buttocks. This contraction may therefore alter the interface pressure distribution. Bogie and Triolo,[4] using implanted electrodes to apply neuromuscular electric stimulation to the gluteal muscles in people with SCI, found an increase in oxygen level (indicative of an improved circulation) in the tissue sur-rounding the ischial tuberosities and an improved interface pressure distribution.

Generally, implanted electrodes are chosen over surface electrodes when large muscles are to be stimulated because surface electric stimulation is often unable to stimulate the contraction, temporarily changing the shape of the buttocks. This contraction may therefore alter the interface pressure distribution. Bogie and Triolo,[4] using implanted electrodes to apply neuromuscular electric stimulation to the gluteal muscles in people with SCI, found an increase in oxygen level (indicative of an improved circulation) in the tissue surrounding the ischial tuberosities and an improved interface pressure distribution.

Generally, implanted electrodes are chosen over surface electrodes when large muscles are to be stimulated because surface electric stimulation is often unable to stimulate the entire muscle belly, even at higher currents. Furthermore, implanted electrodes negate the need for external wires. However, gluteal muscles of persons with SCI are often smaller because of disuse atrophy, and surface electric stimulation might be sufficient for eliciting proper muscle contraction in these persons. In addition, or occasional use, less invasive methods (ie, surface electrodes) may be preferable and serve as an alternative to the implanted electrode system, which also may not be common practice in some countries (eg, because of costs). Therefore, surface electrodes were used to stimulate the gluteal muscles in the present study. Furthermore, possible effects of muscle fatigue were addressed because the distribution of muscle fiber types alters after SCI; the percentage of fast twitch fibers increases,[10] causing less resistance to muscle fatigue in persons with SCI than healthy people. A protocol in which the left and right gluteal muscles were stimulated alternately was compared with a simultaneous stimulation protocol. During the latter, muscles were stimulated twice as often, which may have caused a more rapid onset of fatigue. Both protocols lasted 31 minutes, during which 120 stimulations were applied. Although pressure ulcer prevention

guidelines often suggest lifting or shifting weight every 15 or 30 minutes, this study design may better approach sitting behavior of able-bodied persons, who shift weight constantly to prevent the uncomfortable sensations accompanying tissue compression. Because not only high interface pressure (ie, normal forces) but also shear forces are considered risk factors for developing pressure ulcers, both need to be studied. In this study, the interface pressure under the ischial tuberosities was examined, because this area is considered a high-risk area for the development of pressure ulcers. In addition, the interface pressure distribution and the pressure gradient were used as indicators of shear stress in the soft tissue.[11,12] These outcome measures are somewhat different than current literature. Therefore, maximum interface pressure was also calculated for better comparison.

This study was aimed at the following questions. First, what are the effects of alternating and simultaneous surface electric stimulation of the left and the right gluteal muscles on the pressure in the area under the ischial tuberosities, the maximum pressure, and the interface pressure distribution under the buttocks? Alternating as well as simultaneous surface electric stimulation was expected to cause a decrease in interface pressure in the area under the ischial tuberosities and in maximum pressure, and an improved interface pressure distribution under the buttocks. Second, what are the differences between these 2 stimulation protocols? It was hypothesized that simultaneous surface electric stimulation causes a larger decrease in interface pressure in the area under the ischial tuberosities and in maximum pressure compared with alternating surface electric stimulation. On the other hand, alternating surface electric stimulation was expected to cause less muscle fatigue than simultaneous surface electric stimulation.

Table 1: Participants' Characteristics

Characteristics	Values
Participants (male/female)	13 (12/1)
SCI level	C4-7 (n5)
	T5-11 (n8)
Lesion	Complete (n8) Incomplete (n5)
Age (y)	41.518.2 (20–74)
Time since injury (mo)	87.8103.5 (2–384)
Body mass (kg)	74.112.6 (58–102)
Height (cm)	184.86.0 (174–195)

Note: Values are n or mean SD (range).

Methods

Participants

Thirteen subjects with SCI, with either a complete or an incomplete lesion, participated in this study. All participants had an intact reflex arc, allowing activation of the gluteal muscles by electric stimulation. This was determined by a physician establishing the presence of the Achilles' reflex, the patellar reflex, and the sacral reflexes. Exclusion criteria were the presence of pressure ulcers on the buttocks and intolerance to or contraindication for electric stimulation. Participants' characteristics are summarized in table 1. All participants signed an informed consent before taking part in the study.

General Design

The study was approved by the local institutional review board. Before start of the study, participants were tested to ascertain that surface electric stimulation of the gluteal muscles induced muscle contraction and experimental levels of electric stimulation were tolerated. The study was composed of 1 session consisting of 2 different stimulation protocols. During 1 protocol, left and right gluteal muscles were stimulated alternately, and during the other protocol, the gluteal muscles were stimulated simultaneously. The protocols were applied in a counterbalanced way, with 15 minutes of rest between them. During this session, participants sat in their own daily-use wheelchairs with their regular cushions.

Pressure Mapping

Interface pressure was measured using an Force sensitive array (FSA) consisting of 3232 pressure sensors. Before each measurement, the FSA was calibrated between 0 and 200mmHg. For all measurements, the FSA was placed on the cushion of the wheelchair. Recordings were digitized at a 10- Hz sampling rate. Typical FSA pressure profiles are shown in figure 1 (page 55).

Electric Stimulation

Two 1-channel stimulatorsb were used for the electric stimulation of the gluteal muscles, one for each buttock. The stimulators were synchronized through a personal computer running a custom-built program written in LabView.c Surface electrodesd (80130mm) were placed bilaterally on the gluteal muscles, one at the lower border of the muscle belly and one in the middle of the muscle belly, in order to stimulate the tissue surrounding the ischial tuberosity. To generate a tetanic contraction, rectangular monophasic pulses were applied with 50-Hz stimulation frequency and 80-mA current amplitude.

The alternating stimulation protocol consisted of 0.5-second stimulation of 1 gluteal muscle and a 15-second rest, followed by 0.5-second stimulation of the other gluteal muscle and a 15-second rest. This was repeated 60 times, resulting in a 31-minute protocol. Likewise, the simultaneous stimulation protocol consisted of a 0.5-second stimulation of both gluteal muscles followed by a 15-second rest. This was repeated 120 times, also resulting in a 31-minute protocol.

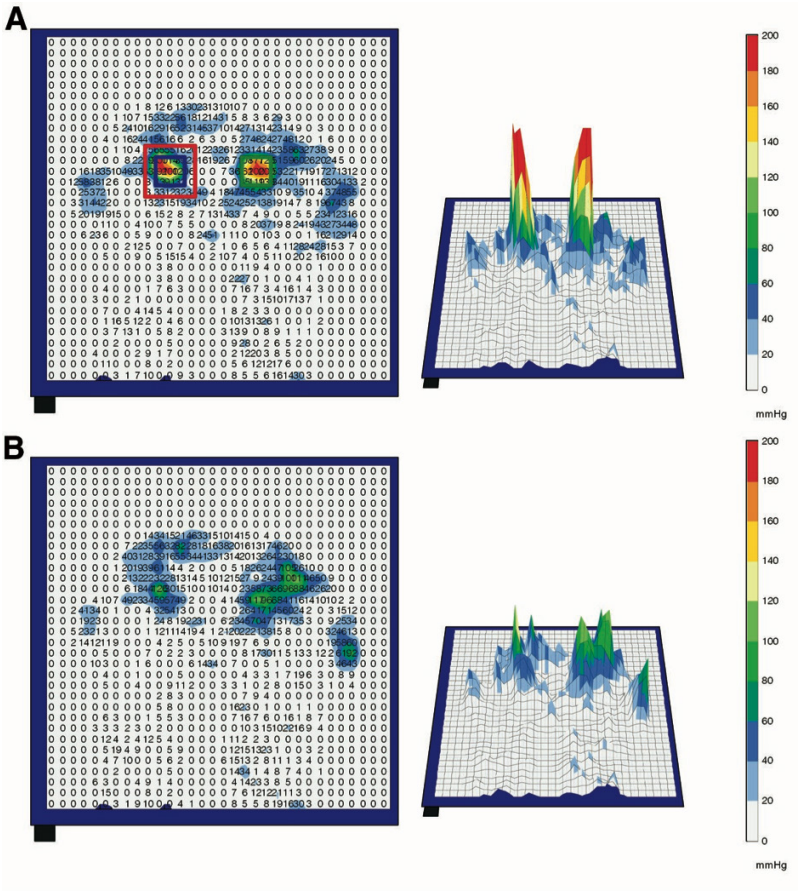

Fig 1.
FSA profiles for 1 participant. The left panels show a 2-dimensional map of interface pressure (ie, a top view); the right panels show a 3-dimensional pressure profile. Images are oriented with the thighs pointing downward. (A) Pressure profile during a rest period of the simultaneous stimulation protocol. The blue and green square indicate the left and right tuber area. The red square denotes the sensors used in computing the pressure gradient. (B) Pressure profile during a stimulation period of the simultaneous stimulation protocol.

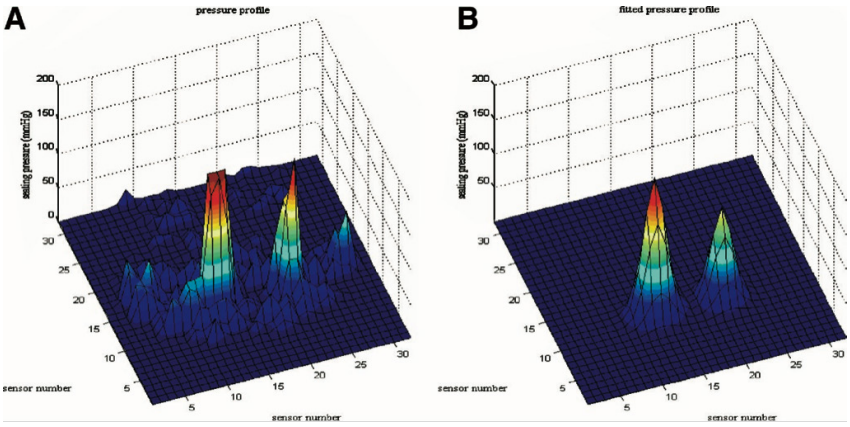

Fig 2.
(A) Interface pressure profiles and (B) the corresponding fit for 1 participant. Images are oriented with the thighs pointing upward to the left.

Outcome Variables

The tuber areas were the areas assumed to correspond to the tissue covering the ischial tuberosities. These areas were defined as the 33 sensor area (matching a 3.63.6cm area) under each buttock with the highest interface pressure during the session (see fig 1A). The tuber areas were determined by visual inspection of the FSA data. The pressure of these 9 sensors was averaged, resulting in a single value for the interface pressure for each tuber area (P). Although this method led to a flattening of the interface pressure, it was used to reduce the loss of data caused by the upper bound of the FSA range; pressures exceeding 200mmHg were clipped and could hence not further be distinguished. Note that the sensor with the highest interface pressure may have exceeded this upper bound. Furthermore, the pressure under the ischial tuberosities was assumed to remain in the tuber areas during small movements, allowing for analyzing the pressure of interest during the entire measurement.

Maximum pressure (M) was calculated for comparison of the present results with current literature. It is defined as the value of the sensor with the highest pressure within the tuber area. The pressure spread (S) was used as a measure for the distribution of the interface pressure. First, the pressure profile obtained from the FSA recordings (fig 2A) was fitted to a Gaussian (ie, normal) distribution (see fig 2B) for each buttock. A Gaussian distribution is defined by its mean (ie, the center of the distribution) and its SD, which determines the width of the Gauss curve (ie, 68.2% of the distribution is contained within the area defined by the mean SD). In this case, the mean was set at the tuber area and the distribution's SD fitted through

the recorded pressure profile. Subsequently, the pressure spread could be defined as 1 SD in 2 directions, anteroposterior and mediolateral, which were averaged for each buttock. A low value for the pressure spread thus corresponds to a narrow Gauss curve, which means that the greater part of the interface pressure (ie, body weight) is supported by a relatively small area of the buttocks (fig 3A). Thus, pressure spread is
an indicator of interface pressure distribution in an area that is larger than just the tuber area (possibly the entire buttock). This might be valuable additional information to measures of peak pressure used in previous studies. Furthermore, a rapid decline in pressure over a small distance is associated with a large shear stress within the buttocks.[11,12] The tissue in this area might be at risk for developing pressure ulcers if the pressure is not relieved regularly.

Fig 3. Gauss curve with (A) a small and (B) a large SD. A narrow Gauss curve corresponds to a low value for the pressure spread (left). The tissue in this area might be at risk for developing pressure ulcers, because the greater part of the interface pressure is supported by a relatively small area and because a rapid decline in pressure over a small distance is associated with a large shear force within the buttocks. An additional measure for the distribution of the interface pressure is its gradient (G)—that is, its derivative with respect to space. Here, we approximated the gradient by the difference in pressure between 2 points, divided by the distance between these points. In more detail, the difference was computed between the mean pressure of the 16 sensors adjacent to sensors of the tuber area and the mean pressure of the 9 sensors of the tuber area (see fig 1A). Because the distance between these groups of sensors was identical for all participants and in all measurements, and because the difference in pressure between these groups is an intuitively comprehensible measure, the choice was made not to divide it by the distance. Therefore, this measure is, strictly speaking, not a gradient, but hints at pressure distribution (changes) next to the mathematically more complicated pressure spread. A high pressure gradient is considered a risk, because high pressure differences over small distances are associated with high shear forces within the tissue. In contrast, lower values are regarded as beneficial. Stimulation measurement. Stimulation periods were determined by visual inspection. To reduce possible errors, interface pressure data from .25 seconds before to (and including) .25 seconds after the determined time frame were averaged for each stimulation period. Likewise, interface pressure during rest periods was computed by averaging data from 6.25 to (and including) 12.5 seconds after each determined time frame.
The difference between the interface pressure (Palt, Psim) during rest periods and during stimulation periods was determined by calculating the mean interface pressure during all rest periods and the mean interface pressure during all stimulation periods. Stimulation of the gluteal muscles of 1 buttock had a similar effect on both the interface pressure under the ipsilateral (ie, the stimulated) buttock and the interface pressure under the contralateral (ie, the not stimulated) buttock. Hence, it was not possible to distinguish between the stimulation of the right buttock and that of the left buttock during the alternating stimulation (fig 4). For this reason, both stimulation protocols were analyzed equivalently. Fatigue may generally

result in a less forceful contraction leading to a diminished temporary change in the shape of the buttocks. This in turn may be reflected in a reduced decrease in interface pressure caused by electric stimulation. To determine whether effects of stimulation (Palt, Psim) changed during 30 minutes of stimulation, the difference between the interface pressure during stimulation periods and rest periods in the first 2.5 minutes of the measurement was compared with the difference between the interface pressure during stimulation periods and rest periods in the last 2.5 minutes of the measurement.

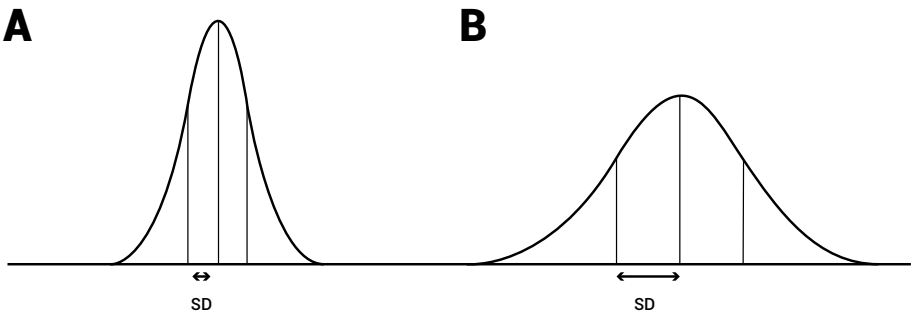

Fig 3.
Gauss curve with (A) a small and (B) a large SD. A narrow Gauss curve corresponds to a low value for the pressure spread (left). The tissue in this area might be at risk for developing pressure ulcers, because the greater part of the interface pressure is supported by a relatively small area and because a rapid decline in pressure over a small distance is associated with a large shear force within the buttocks.

The 2 stimulation protocols were compared by determining the difference between P_{alt} and P_{sim} (ie, the difference in instantaneous effect of stimulation periods, P_{effect}) and the difference between P_{alt} and P_{sim} (ie, the difference in change in effect of stimulation periods after 30 minutes, P_{effect}). In line, these 6 variables were calculated for the maximum pressure, the pressure spread, and the pressure gradient (M_{alt}, M_{sim}, M_{alt}, M_{sim}, M_{effect}, M_{effect}, S_{alt}, S_{sim}, S_{alt}, S_{sim}, S_{effect}, S_{effect}, G_{alt}, G_{sim}, G_{alt}, Gsim, G_{effect}, G_{effect}).

Statistical Analysis

Interface pressure, maximum pressure, pressure spread, and pressure gradient were compared using 2-tailed paired t tests. All results are presented as mean SD. The level of significance of all analyses was set at equal to .05.

Results

Both during the stimulation periods and during the rest periods, there was no significant difference between left and right interface pressure, between left and right maximum pressure, between left and right pressure spread, and between left and right pressure gradient during both stimulation protocols. The average of the values for left and right buttock was calculated and used for statistical analysis.

Table 2: Differences in Interface Pressure (in mmHg), Pressure Spread (in number of sensors), Pressure Gradient (in mmHg), and Maximum Pressure (in mmHg) Between Rest Periods and Stimulation Periods of Measurements for Alternating and Simultaneous Protocols

Pressure	Rest SD	Stimulation SD	Difference SD	P
P_{alt}	10630	8830	1712	.001*
S_{alt}	3212	3715	511	.123
G_{alt}	6546	5341	1211	.002*
M_{alt}	14240	12237	2116	.001*
P_{sim}	10030	8133	1914	.001*
S_{sim}	3412	4738	1434	.197
G_{sim}	6752	5346	1412	.001*
M_{sim}	12834	10336	2519	.001*

Abbreviations: G_{alt}, pressure gradient during the alternated stimulation protocol; G_{sim}, pressure gradient during the simultaneous stimulation protocol; M_{alt}, maximum pressure during the alternated stimulation protocol; Msim, maximum pressure during the simultaneous stimulation protocol; P_{alt}, interface pressure during the alternated stimulation protocol; Psim, interface pressure during the simultaneous stimulation protocol; S_{alt}, pressure spread during the alternated stimulation protocol; Ssim, pressure spread during the simultaneous stimulation protocol. *Significant.

During simultaneous stimulation, the interface pressure (P_{sim}) decreased from 10030mmHg in rest periods to 8133mmHg in stimulation periods (P.001) (see table 2). Maximum pressure (M_{alt}, M_{sim}) decreased during both alternating (–2116mmHg, P.001) (see table 2) and simultaneous (–2519mmHg, P.001) (see table 2) stimulation protocols. In both protocols, the pressure spread (S_{alt}, S_{sim}) did not differ significantly between rest periods and simultaneous stimulation periods (P.123, P.197 respectively) (see table 2). For the alternating stimulation, the pressure gradient (G_{alt}) decreased from 6546mmHg during rest periods to 5341mmHg during stimulation periods (P.002) (see table 2). During the simultaneous stimulation, the pressure gradient (G_{sim}) changed from 6752mmHg in rest periods to 5346mmHg in stimulation periods (P.001) (see table 2). During both alternating and simultaneous stimulation, the difference in interface pressure (P_{alt}, Ps_{im}), the difference in pressure spread (S_{alt}, S_{sim}), and the difference in pressure gradient ($G_{alt,}$ G_{sim}) between beginning and end of the protocol did not change significantly (table 3). Maximum pressure did not change between the beginning and the end of the alternating stimulation protocol (M_{alt}), but decreased –24mmHg (P.04) (see table 3) from beginning to end of the simultaneous stimulation protocol (M_{sim}).

Remarkably, during measurements, for most subjects, at least 1 of the pressure sensors showed the maximum value of 200mmHg despite the use of personal wheelchairs and personal cushions (individually assigned/designed for optimal pressure distribution). However, this strengthened the decision to average the values of the 9 sensors constituting the tuber area During alternating stimulation, the interface pressure (Palt) changed from 10630mmHg in rest periods to 8830mmHg in stimulation periods (P.001) (table 2).

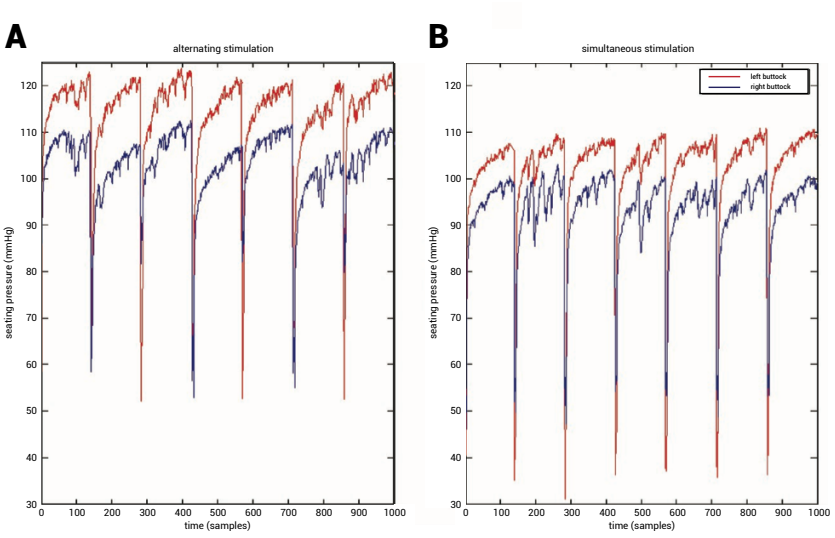

Fig 4.
Time series of the interface pressure during the (A) alternating and (B) simultaneous stimulation protocol for 1 participant.

Stimulation Protocols

The 2 protocols did not differ significantly for the difference in interface pressure (P_{effect}), the difference in pressure spread (S_{effect}), and the difference in pressure gradient (Geffect) between rest periods and stimulation periods, although there was a tendency for the simultaneous stimulation protocol to have a larger decrease in interface pressure (P.091) (table 4).

The difference in effect of the electric stimulation (P_{effect}, S_{effect}, G_{effect}) between the beginning and the end of the measurement did not differ significantly between the protocols (see table 4).

Discussion

The present study was aimed at investigating the effects of surface electric stimulation of the gluteal muscles on the inter- face pressure distribution in patients with SCI. During the alternating and simultaneous electric stimulation protocol, the expected reduction in interface pressure during stimulation periods could be observed. On average, the interface pressure during these periods decreased 17 and 19mmHg (alternating stimulation and simultaneous stimulation, respectively).

This pressure-reducing effect did not change in the course of the 30 minutes of electric stimulation application. For this period, the gluteal muscles (and the surrounding tissue) may thus benefit from pressure relief caused by their own contractions without noticeable muscle fatigue. Although there was a tendency for the simultaneous protocol to have a larger decrease in interface pressure, the difference in effect between the 2 protocols was 2mmHg, which appears clinically irrelevant.

Next to the 9-cell interface pressure, maximum pressure was calculated as a single-cell measure for comparison with current literature. This parameter showed larger effects of the alternating and simultaneous stimulation protocol (–2116mmHg, –2519mmHg, respectively) than the interface pressure parameter. This could confirm the expectation that averaging the values of 9 sensors leads to a flattening of the interface pressure. Contrary to the interface pressure, maximum pressure showed a significant decrease between the beginning and the end of the simultaneous stimulation measurement. However, this decrease was small (–24mmHg) and might not be clinically relevant.

Using implanted electrodes for neuromuscular electric stimulation of the gluteal muscles, Bogie and Triolo4 found a decrease in ischial region interface pressure. In contrast with the present study, this decrease occurred while sitting without electric stimulation after an 8-week conditioning training of the stimulated muscles, which may have changed muscle mass and thus the shape of the buttocks.

That is, no instantaneous effects (ie, the direct effect of muscle contractions) of electric stimulation were reported. In a more recent case study, Bogie et al[13] used the same electric stimulation system and found a similar long-term effect on interface pressure as well as instantaneously increased pressure variations during an alternating stimulation protocol (up to 10h/d of 15-second stimulation/15second rest for a 3-minute period followed by a 17-minute interstimulation interval). Liu et al[14] established contractions of gluteal muscles by S2 nerve root stimulation in 5 subjects with SCI and a sacral anterior root stimulator implant. This caused a reduction in the ischial tuberosity peak pressure of 4926mmHg, which is about twice as large as in the present study. This difference might be explained by the fact that nerve root stimulation activates the entire neuromuscular bundle, whereas surface stimulation often reaches only part of the muscle. Another factor contributing to the difference may be the use of other methods of calculation. In the present study, interface pressure data from .25 seconds before to (and including) .25 seconds after the determined time frame of a stimulation period were averaged, which may have included data from rest periods. Furthermore, interface

Table 3: Differences () in Interface Pressure (in mmHg), Pressure Spread (in number of sensors), Pressure Gradient (in mmHg), and Maximum Pressure (in mmHg) Between Beginning and End of Measurements for Alternating and Simultaneous Protocols

Pressure	Beginning SD	End SD	Difference SD	P
P_{alt}	1813	1713	15	.302
S_{alt}	611	57	15	.570
G_{alt}	1411	1212	14	.276
M_{alt}	2216	1916	25	.116
P_{sim}	2014	1914	13	.116
S_{sim}	1632	1632	06	.940
G_{sim}	1511	1411	13	.397
M_{sim}	2621	2424	24	.040*
M_{sim}	12834	10336	2519	.001*

Abbreviations: G_{alt}, difference in pressure gradient between rest and stimulation periods during the alternated stimulation protocol; G_{sim}, difference in pressure gradient between rest and stimulation periods during the simultaneous stimulation protocol; M_{alt}, difference in maximum pressure between rest and stimulation periods during the alternated stimulation protocol; M_{sim}, difference in maximum pressure between rest and stimulation periods during the simultaneous stimulation protocol; P_{alt}, difference in interface pressure between rest and stimulation periods during the alternated stimulation protocol; P_{sim}, difference in interface pressure between rest and stimulation periods during the simultaneous stimulation protocol; S_{alt}, difference in pressure spread between rest and stimulation periods during the alternated stimulation protocol; S_{sim}, difference in pressure spread between rest and stimulation periods during the simultaneous stimulation protocol. *Significant.

Table 4: Differences () in Reducing Effect on Interface Pressure (in mmHg), Pressure Spread (in number of sensors), Maximum Pressure (in mmHg), and Pressure Gradient (in mmHg) Between Simultaneous and Alternating Stimulation Protocols

Pressure	Alternating SD	Simultaneous SD	Difference SD	P
P_{effect}	1712	1914	24	.091
S_{effect}	511	1434	924	.219
G_{effect}	1211	1412	15	.343
M_{effect}	2621	2216	416	.336
P_{effect}	15	13	06	.990
$S_{effec}t$	15	06	18	.666
G_{effect}	14	14	15	.675
M_{effect}	12	13	02	.877
M_{sim}	12834	10336	2519	.001*

Abbreviations: G_{effect}, reducing effect caused by electric stimulation on pressure gradient; G_{effect}, difference in reducing effect caused by electric stimulation on pressure gradient between the beginning and the end of the measurement; M_{effect}, reducing effect caused by electric stimulation on maximum pressure; Me_{ffect}, difference in reducing effect caused by electric stimulation on maximum pressure between the beginning and the end of the measurement; P_{effect}, reducing effect caused by electric stimulation on interface pressure; P_{effect}, difference in reducing effect caused by electric stimulation on interface pressure between the beginning and the end of the measurement; S_{effect}, reducing effect caused by electric stimulation on pressure spread; S_{effect}, difference in reducing effect caused by electric stimulation on pressure spread between the beginning and the end of the measurement.

pressure exceeding 200mmHg could not be detected because of the limits of the FSA, rendering changes in this range unnoticed.

Levine et al[15] applied surface electric stimulation to the gluteal muscles of 3 able-bodied subjects while seated on different interface surfaces. Reductions in interface pressure under the ischial tuberosities were consistently established during stimulation, although the magnitude of change depended on the interface surface, and an effect of percentage of buttock adipose tissue was suggested. It was hypothesized that "the results should extend to paralysed individuals with appropriately conditioned muscle,"[15] which implies that most people with SCI would require a training period before the electric stimulation becomes useful. However, the present study showed a decrease in interface pressure under the ischial tuberosities during surface electric stimulation despite the participation of a group with varying degrees of atrophy. It seems that muscle condition for people with and without paralysis cannot be straightforwardly compared.

In the present study, the interface pressure distribution was expected to improve because of electric stimulation, meaning higher values for pressure spread and lower values for pressure gradient. In both types of stimulation, the pressure spread remained by and large constant, but the pressure gradient dropped. Recall that the pressure spread indicates the interface distribution of the entire buttock, whereas the pressure gradient reflects the interface pressure distribution of the area directly surrounding and containing the tuber area. Only the latter improved, and the fact that pressure spread did not alter suggests that the elicited muscle contractions did not change the shape of the entire buttock. In the aforementioned study using surface electric stimulation of the gluteal muscles of 3 ablebodied subjects by Levine,[15] a change in pressure distribution during muscle contractions was found: interface pressure under the ischial tuberosities decreased and pressure in the surrounding areas increased. The difference in calculating the outcome variables between this and the present study, however, renders a further comparison difficult. In subsequent research, Levine et al16 found a change in tissue shape at the interface during electric stimulation of the gluteal muscles, but this study—like the previous one—included only able-bodied subjects. In the present study, subjects with SCI participated with varying degrees of atrophy of the gluteal muscles. With less muscle mass present to deform, only limited (or no) variations in shape can be expected, which is reflected in the unchanged pressure spread. When comparing the alternating stimulation protocol with the simultaneous stimulation protocol, no differences were found with respect to the effects on interface pressure and pressure distribution and with respect to the time these effects last. It was expected that simultaneous electric stimulation would cause a larger decrease in interface pressure and that alternating stimulation would cause less muscle fatigue. Therefore, for a period of 30 minutes, the choice for alternating or simultaneous electric stimulation to reduce interface pressure will be arbitrary. For longer protocols, however, one may still expect that alternating stimulation causes less fatigue because the contraction frequency of the gluteal muscles in this protocol is only half of the contraction frequency during simultaneous stimulation.

The present study was based on the following assumptions. First, it was assumed that the 33

sensor area designated as tuber area actually contained the area under the ischial tuberosity and that this was a high-risk area for developing pressure ulcers. Although the calculated tuber area might be somewhat larger than the tuberosity itself, this size was chosen to make sure the ischial tuberosity was still within this area even when muscle contractions caused (minimal) displacement. Second, it was assumed that the pressure measured with the FSA corresponds to the pressure at the interface and that this, in turn, is an indication of the pressure within the tissue (which can be a risk factor for pressure ulcers when it is high or is not relieved regularly). Although Linder-Ganz et al[17] measured lower pressure at the interface than in the underlying tissue (it was highest in muscle tissue), the gluteal muscle mass is small because of disuse in most people with SCI, and the tissue covering the ischial tuberosities is very thin. Therefore, no large differences between pressure superficially and pressure deeper within the tissue were expected. Third, it was assumed that pressure spread and pressure gradient are indicators of pressure distribution and shear force, as discussed (see Methods section and fig 3). Together these variables (interface pressure, maximum pressure, pressure spread, pressure gradient) were assumed to affect soft tissue stresses and blood flow, and thereby the risk of developing pressure ulcers.

Study Limitations

The following limitations might have confounded this study. There was considerable variation in participants' characteristics (see table 1) and in their compliance to the instruction to sit as still as possible during measurements. Although it might be possible to recruit a more homogeneous group of participants, it will be difficult to control temperament. Some people had sensory-incomplete SCI, but all participants tolerated the same levels of electric stimulation well. Level and (motor) completeness of injury in all participants was such that the gluteal muscles were paralysed (see table 1). Differences in
interface pressure among subjects have probably been caused by the fact that each participant sat in his personal wheelchair with his personal cushion. Intersubject variability in interface pressure is caused by differences in patient weight, cushion stiffness, and size and shape of the support area.[18,19] Levine[15] found that the effect of electric stimulation depends on the compliance of the interface surface. However, these variations in patient and wheelchair characteristics have had little influence on the outcome of this study, because only changes in interface pressure were considered, and no comparisons among subjects were made. Moreover, it is interesting to evaluate the additional effect of electric stimulation on interface pressure besides the effect of individually adjusted wheelchairs and cushions. A phenomenon that might have affected measurements is the process of tissue compression: the continuous pressure of body weight pushes the ischial tuberosities deeper into the tissue of the buttocks, which gradually deform, causing a continuous change in pressure (distribution). This process was studied in an earlier pilot (unpublished) in which the same subjects as in the present study sat as still as possible for 90 minutes. A gradual rise in interface pressure was found that lasted

on average 30 minutes, but for 10 subjects, it lasted nearly an hour. Other limitations to the present study were mostly technical limitations—for example, the 200-mmHg limit of the FSA, because of which no pressure changes could be observed above 200mmHg.

The rationale in this study for using electric stimulation in the prevention of pressure ulcers was the expectation that a reduction in interface pressure might undo the occlusion of blood vessels and restore blood flow to tissue at risk. Several studies on interface pressure thresholds for development or prevention of pressure ulcers have been conducted,[20,21] but none could establish absolute values for these thresholds. Therefore, it is not clear whether the interface pressure reduction found in the current study is sufficient for pressure ulcer prevention. Furthermore, other factors besides absolute interface pressure (reduction) affect the restoration of blood flow and tissue oxygenation. First, Coggrave and Rose[22] showed that during passive pressure relief by subjects with SCI, it takes about 2 minutes to restore tissue oxygen levels to unloaded values. During electric stimulation, however, tissue oxygenation might develop faster because of muscle contractions and the skeletal muscle pump mechanism. Second, people with and without SCI show different responses in the periodic oscillations of blood flow after the release of occlusive pressure.[23] However, in healthy people, even 3-Hz twitch contractions increase leg blood flow in uncompressed tissue while in a supine position,[24] and 0.5-second tetanic contractions in people with SCI might induce similar effects. In addition, during the stimulation protocols of the current study, the muscles showed no sign of fatigue, which indicates that sufficient blood was brought to the muscles to endure the number of contractions. To determine the effect of electric stimulation on blood flow and tissue oxygenation directly and to study possible relationships between interface pressure and blood flow and tissue oxygenation during stimulation, methods for assessing tissue oxygen levels should be combined with interface pressure mapping and electric stimulation.

Electric stimulation protocols in this study lasted 30 minutes, during which 120 stimulations were applied. Although pressure ulcer prevention guidelines often suggest lifting or shifting weight every 15 or 30 minutes, this study design may better approach sitting behavior of able-bodied persons, who shift weight constantly to prevent the uncomfortable sensations accompanying tissue compression. For those with SCI, it may be impossible (or at least impractical) to lift or shift weight this often, but 2 to 4 times an hour, on the other hand, may be insufficient. In addition, frequent lifting may promote shoulder injuries because of high contact forces within the glenohumeral joint.[7] The present protocol design was a pilot, which has been demonstrated to be effective for the duration of 30 minutes without muscle fatigue. Other (eg, longer, more elaborate) protocols need to be tested to establish the most practical and effective electric stimulation protocols.

Electric stimulation of paralysed muscles in people with SCI not only temporarily decreases interface pressure, possibly restoring blood flow, but also has long-term positive effects on tissue health such as reduction of atrophy and elevating tissue oxygen levels.[4,8,9] These structural changes might constitute an even more effective prevention of pressure ulcers, because underlying factors contributing to the development of pressure ulcers are addressed.

Therefore, the method of automatically applied external stimulation and pressure relief used in this study could well be a new approach of pressure ulcer prevention besides the application of specially designed cushions and protective behavior.

Because of these positive long-term effects on tissue health,[4,8,9] it would be interesting to study training effects of repeated application of electric stimulation protocols further. Other aims for further research will be protocols with different stimulation and rest cycles, the onset of muscle fatigue in stimulation protocols lasting longer than 30 minutes, the instantaneous effects of surface electric stimulation on blood flow and tissue oxygen levels, possible neural adaptation to electric stimulation, individually adapted current amplitudes, and practical adaptations for easier application in the clinic or at home (eg, pants with built-in electrodes).

Conclusions

Alternating and simultaneous stimulation protocols have similar effects during 30 minutes, without noticeable muscle fatigue: interface pressure is reduced during stimulation periods, but pressure distribution does not change.

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Suppliers

a. FSA, Vista Medical, Unit #3 – 55 Henlow Bay, Winnipeg, MBR3Y 1G4, Canada.
b. DS7A; Digitimer Ltd, 37 Hydeway, Welwyn Garden City, Hert-fordshire, AL7 3BE, UK.
c. National Instruments, 11500 N Mopac Expwy, Austin, TX 78759-3504.
d. Schwa-Medico, De Biezenkamp 4, Leusden 3831 JA, The Nether-lands.

4

Effects of electrical stimulation-induced gluteal versus gluteal and hamstring muscles activation on sitting pressure distribution in persons with a spinal cord injury

CAJ Smit, GLG Haverkamp, S de Groot, JM Stolwijk-Swüste and TWJ Janssen

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ABSTRACT

Study design: Ten participants underwent two electrical stimulation (ES) protocols applied using a custom-made electrode garment with built-in electrodes. Interface pressure was measured using a force- sensitive area. In one protocol, both the gluteal and hamstring (g+h) muscles were activated, in the other gluteal (g) muscles only.
Objectives: To study and compare the effects of electrically induced activation of g+h muscles versus g muscles only on sitting pressure distribution in individuals with a spinal cord injury (SCI).
Setting: Ischial tuberosities interface pressure (ITs pressure) and pressure gradient.
Results: In all participants, both protocols of g and g+h ES-induced activation caused a significant decrease in IT pressure. IT pressure after g+h muscles activation was reduced significantly by 34.5% compared with rest pressure, whereas a significant reduction of 10.2% after activation of g muscles only was found. Pressure gradient reduced significantly only after stimulation of g+h muscles (49.3%). g+h muscles activation showed a decrease in pressure relief (D IT) over time compared with g muscles only. Conclusion: Both protocols of surface ES-induced of g and g+h activation gave pressure relief from the ITs. Activation of both g+h muscles in SCI resulted in better IT pressure reduction in sitting individuals with an SCI than activation of g muscles only. ES might be a promising method in preventing pressure ulcers (PUs) on the ITs in people with SCI. Further research needs to show which pressure reduction is sufficient in preventing PUs.

Keywords: spinal cord injury; pressure ulcers; electrical stimulation; sitting pressure

Introduction

Pressure ulcers (PUs) are serious and costly complications for people with a spinal cord injury (SCI), occurring in up to 80% of cases.[1,2] A PU is an area of localized damage to the skin and underlying deeper tissue caused by unrelieved pressure, shear, friction or a combination of these.[3] The most common areas for PUs for individuals with SCI are the sacrum and ischial tuberosities (ITs), which account for approximately 50% of incidents.[4] Prevention of PUs in SCI is therefore of utmost importance.

Muscle contractions induced by electrical stimulation (ES) might help prevent PUs as they improve both the intrinsic risk factors for developing PUs, because ES may reduce atrophy,[5] improve blood flow and oxygenation,[6,7] and sitting pressure distribution as it redistributes pressure away from the ITarea.8 Levine et al.[6–8] found that surface ES of the gluteal (g) muscles produces a sizeable pressure reduction below the ITs. In addition, Ferguson et al.[9] noted reduced sitting pressure after stimulating the quadriceps while the lower legs were attached to the cranks of the footrests. Liu et al.[10] studied the acute effects of ES of the g muscles, using implanted electrodes, resulting in clinically significant reductions in IT pressures. In conclusion,

one could maintain that ES might help preventing PUs in the IT region.
In line with these findings, in a previous study in our research lab Van Londen et al.[11] showed that activation of g muscles relocates pressure from the ITs. However there were limitations and topics for further research in this study, as only g muscles were stimulated, and participants were sitting on the electrodes, which is, of course, an undesirable situation. In this study, we compared the effects on sitting pressure and pressure distribution between g muscle activation versus both gluteal and hamstring (g+h) muscles activation. The hamstring muscles have an extension moment in the hip joint and we expect to find that contraction of both g+h muscles changes the shape of the buttocks in another, possibly better way than stimulation of the g muscles only. On the other hand, we wondered if the electrical intensity would be sufficient when the large hamstrings were activated. Furthermore, in this study electrodes were placed halfway up the hamstrings and above the sitting surface at the g muscles. The electrodes were fitted inside a newly developed garment or shorts (ES shorts), which prevent participants who are wearing the shorts from sitting on electrodes or wires. This gave rise to the question if it would be possible to adequately activate two large muscles with only two electrodes, without complications.

This study aimed to answer two questions:
1. What are the acute effects of 1h of ES-induced (g+h or g) muscles activation on interface pressure distribution in sitting individuals with SCI?
2. Do the effects of two stimulation protocols on interface pressure differ over time?

Materials and Methods

Participants

Ten individuals with an SCI, having a complete or incomplete upper-motor neuron lesion (ASIA A, B or C), aged 34 (±9) years, with intact g+h muscles participated. Exclusion criteria were the presence of PUs on the buttocks, a flaccid paralysis (areflexia), intolerance to or contra-indication for ES, a history of severe autonomic dysreflexia or severe cognitive or communicative disorders. The study was approved by the local institutional review board and participants signed an informed consent form. Participants characteristics in Table 1.

Study design

Two different 1-h stimulation protocols were performed in one session. Each participant had to put on the ES shorts and was allowed to wear normal pants over them. Participants all used their own wheelchair with a regular cushion. In Figure 1, these ES shorts with electrical stimulator are shown.

Both protocols consisted of four blocks of 3-min stimulation (t0, t1, t2 and t3) and 16+1min of rest in between blocks (Figure 2). Pressure values were recorded during the 3min of stimulation and during the last minute of the preceding rest period. A duty cycle of 1-s stimulation and 4-s off was performed within the 3min of ES. Stimulation–rest ratio was identical for both protocols. First g muscles were stimulated and then g+h. There was a 30-min rest period in between protocols.

ES with the ES shorts

The ES shorts (Axiobionics, Ann Arbor, MI, USA) were custom-developed lycra shorts in which wires and surface electrodes had been processed. Two built-in surface electrodes are placed over g muscles and over h muscles, on both sides (Figures 1 and 2). The surface electrodes (with conductive gel) are connected to elastic conductors, guided through the side of the shorts to the front, ensuring the participant does not sit on these wires. An eight-channel electrical stimulator (Neuropro, Berkelbikes Nijmegen, The Netherlands) connected to the shorts was used. The standard stimulator potential is 150V. Stimulation was delivered biphasically at 50Hz to induce a tetanic contraction. First the g muscles were activated, and then the same absolute amplitude was also used for activation of g+h muscles of that individual. The current amplitude was adjusted for each subject by increasing the current amplitude in steps of 5mA, while recording interface sitting pressure, until the best reduction ES). In Figure 6, an overview of 64min of measurements is shown. in sitting pressure, without discomfort or excessive muscle contractions was found. The average current amplitude was 94±12.5mA, ranging from 70 to 115mA.

Table 1: Subjects' characteristics

	Mean±s.d. (range)
Age (years)	33.7±8.9 (22–54)
Lesion level	C3–C8 (n¼8) Th1-Th12 (n¼2)
Asia impairment score	Asia A; n¼8 Asia B; n¼1 Asia C; n¼1
Time since injury (months)	55±63 (6–173)
Body mass (kg)	76.0±13.5 (60–99)
Height (m)	1.75±0.31 (1.71–2.01)

Figure 1.
ES-shorts connected with the eight-channel Neuropro stimulator; front and back.
Arrows indicate the electrodes for right g+h muscles.

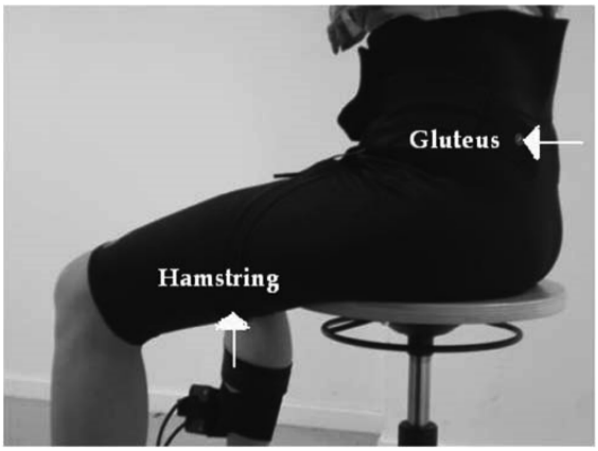

Figure2.
Arrows indicate the position of electrodes in the ES shorts.

Interface pressure measurements

Interface sitting pressure was measured using a force-sensitive array (FSA, Vista Medical, Vancouver, Canada). In this, thin 4242cm soft flex mat 256 pressure sensors (1.82cm2 per sensor) have been incorporated. It was calibrated between 0 and 200mmHg according to the systems protocol. From each of the eight FSA recordings per participant, the mean IT pressure and pressure gradient were calculated. The ITs were defined by inspection of the FSA profiles and selecting the 33 sensors with the highest pressure values, from which the mean (left and right) IT pressure was calculated (IT pressure) (Figure 3). The pressure gradient was calculated by subtracting the average of the 16 surrounding sensor values from the IT pressure. This pressure gradient may indicate shear forces and a high pressure gradient is associated with high shear forces within the tissue, increasing the risk of developing PUs.

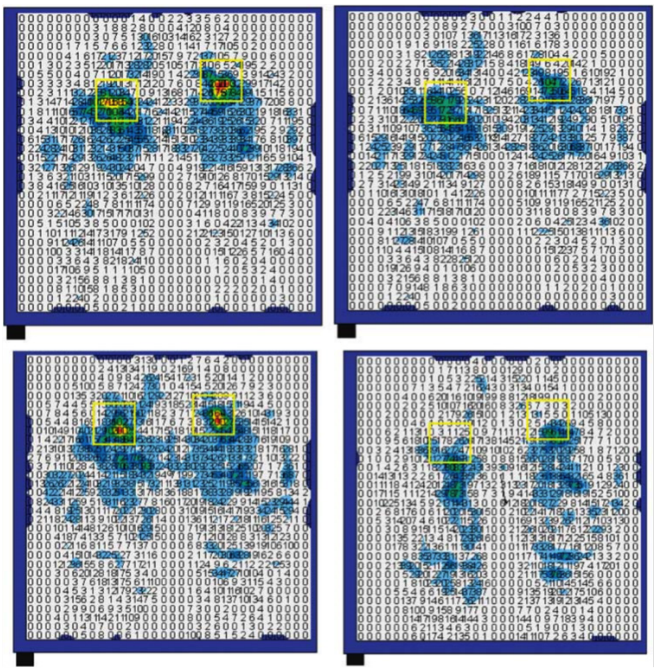

Figure 3.
FSA frames of interface pressure distribution as a two-dimensional map. The highest pressure values represent the ITs. Recordings of one participant during rest (above left and below left), and during activation of g muscles (above right) and both g+h muscles (below right). The squares in left frames indicate the 33 sensor areas with the highest pressure values (ITs). In the right frames, pressure is relocated after muscle activation

Data analysis

The acute effects of the stimulation were investigated by calculating the mean ITand gradient pressures, by averaging all the recorded pressures during the 3min stimulation blocks (1-s stimulation, 4-s rest). In total, this resulted in 8 times 36 recordings of ES-induced activation, which were added to the pressures of 8 times 144 recordings in rest. In Figures 4 and 5, these are compared with pressures in rest (no Spinal Cord DIT and Dpressure gradient were calculated by subtracting the mean values with ES from these pressure values during the preceding rest (¼no ES). This resulted in variables DIT and Dpressure gradient at t0, t1, t2 and t3 for both protocols (g, and g+h).

Statistical analysis

SPSS for Windows software (version 16.0, Chicago, IL, USA) was used to analyze the data collected with the FSA. All results were described as mean±s.d. A paired samples t-test was performed, comparing the IT pressure and pressure gradient of the values in rest with the average of the pressures during stimulation.

A general linear model analysis of variance with repeated measures was used to analyze the effect of time within both protocols (factor: time (n¼4) per protocol). To analyze the differences between activation of the g+h muscles and activation of the g muscles only over time (interaction effect 'time protocol') a second general linear model analysis of variance with repeated measures was performed with two within factors: time (n¼4), and protocol (n¼2). Differences with a P-value p0.05 were considered significant

Results

Both g and g+h muscle activation gave significant IT pressure relief compared with rest. When averaging all pressure values, activation of g+h muscles gave significantly more pressure relief from the ITs than activation of g muscles only (37.8±23.2 versus 11.8±11.7mmHg). The average pressure gradient only reduced significantly over time for the stimulation of both the g+h muscles (14.7±17.1 versus 5.3±9.2; Figures 4 and 5). Mean between group difference: 25.9 (confidence interval: 14.6–37.3mmHg).

DIT showed no significant change over time for g muscle activation only, but significantly decreased over time for activation of g+h muscles: from 44.0mmHg at t0 to 28.5mmHg at t3 (P¼0.01).

DPressure gradient showed no significant change from 18.4mmHg at t0, to 8.2mmHg (55.4%) at t3 (P¼0.10) during activation of both g+h, nor for activation of g only (6.5mmHg at t0 to 4.3mmHg (66.2%) at t3) (P¼0.65) (Table 2).

There was no significant interaction effect between the stimulation protocols and the moments of time. When activating both g+h muscles, neither the IT pressure (P¼0.28) nor pressure gradient (P¼0.41) changed differently over time compared with activation of the g muscles only (Table 2).

Discussion

Both protocols induced significant reductions of pressure at the ITs, but activation of both the g+h muscles resulted in larger pressure reductions. This is likely caused by changes in tone and shape of the activated muscles, with larger effect when adequately activating more muscles (g+h), in combination with the extension in the hip with lifting effect, by activation of the hamstrings.

We compared our results with other studies, such as the study by Van Londen et al.[11] In that study, IT pressure reductions found during ES (mean 19.0mmHg), were better than the results for stimulation of the g muscles only in this study (11.8mmHg). The pressure gradient reduced 14.0mmHg in the study of Van Londen et al. while in this study the pressure gradient reduced 5.3mmHg. This difference may be caused by the use of a different stimulation protocol, as Van Londen et al. stimulated with a stimulation– rest cycle of 0.5-s on and 15-s off, and also by the electrodes that were positioned for each participant individually, whereas in this study the electrodes were fixed to one place in the only pair of shorts used.

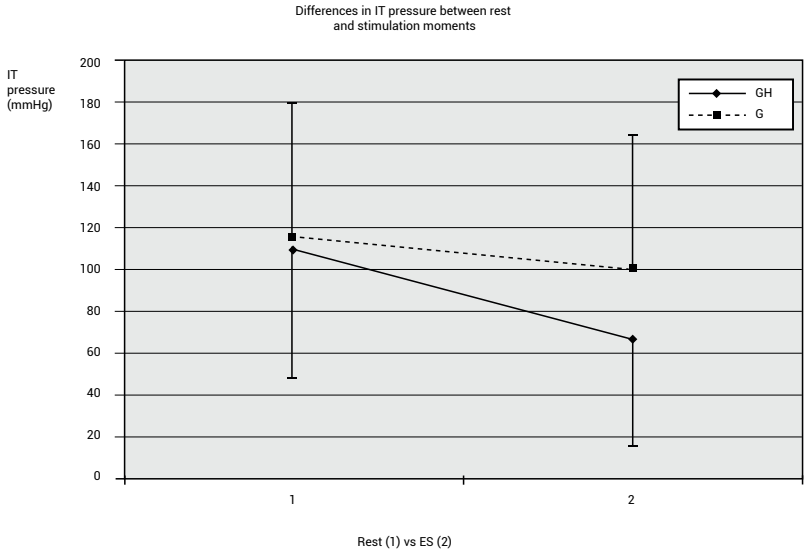

Figure 4.
Average IT pressure in rest and after activation of both the g+h muscles or the g muscles only.

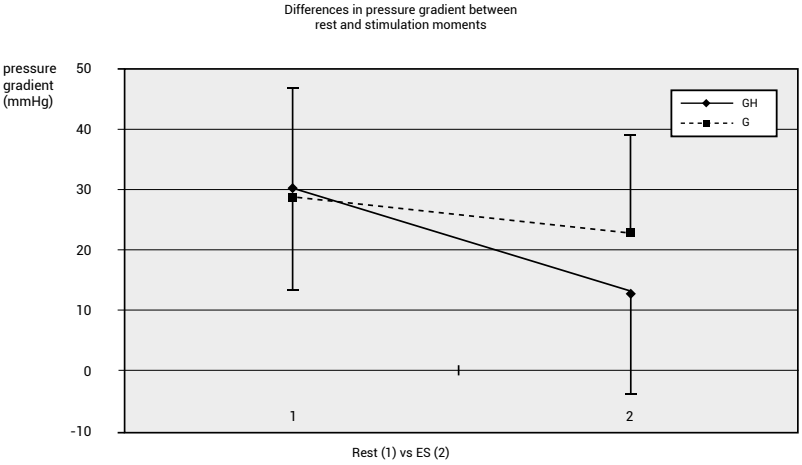

Figure 5.
Average pressure gradient in rest and after activation of both the g+h muscles or the g muscles only.

If, in the future these shorts were to be tailor made, the effect could increase even more, as not only the electrodes in the shorts would then be individually positioned, but also the better stimulation–rest ratio would be used. In this study, g+h muscles activation showed larger reductions compared with Van London (IT pressure reduction 37.8mmHg and in pressure gradient 14.7mmHg versus Van Londen: 19.0 and 4.0mmHg). Ferguson et al.[9] studied the effect of functional ES on the quadriceps muscles, with both feet fixed on the footrests. The average pressure drop when activating both legs was 35.5mmHg.

This reduction is higher than achieved by activating the g muscles only, but approximately the same compared with g+h activation. One can conclude that ES-induced surface activation of both g+h muscles is an effective manner for reducing pressure from the ITs, more effective than only g muscle activation.

In this study, while activating g+h muscles, an increase in pressure was seen in the area of the upper legs, as the pressure was relocated from the ITs to the front of the sitting surface. This (desirable) relocation did not cause any skin problems in this area, as there are no bony prominences at the hamstring site near the knees.[12,13] DIT showed no significant change over time for g muscle activation only, but significantly decreased over time for activation of g+h muscles. But DIT for g+h activation was higher than g muscle activation at T0 (44.0 versus 14.7mmHg), and at T3 (28.5 versus 7.6mmHg). Therefore, a larger decline but 'higher start and end' pressure difference between activation and rest for g+h versus g muscle activation was found. The decline over time might be caused by less forceful contractions because of muscle fatigue after repetitive activation. This needs further investigation.

We also wondered what effects training of these muscles will have, as we hypothesize that ES training might reduce the negative effects of fatigue.[14,15] In literature, no studies were found describing effects of ES training on fatigue or sitting pressure in people with SCI or other diagnose groups.

The best current was determined for each participant by first activating g muscles up to a maximum, with effective contractions without discomfort. The current amplitude for that individual was then kept equal for the activation of the g+h muscles. The effect of the stimulation was higher when stimulating both the g+h muscles, no matter what current was used. We expected a higher current would be needed for activation of g+h compared with g muscles only, as a larger muscle volume had to be activated, but this expectation proved incorrect. It appeared that activation with equal currentboth protocols g and g+h muscle activation at several moments in time amplitude of g+h muscles compared with activation of g muscles only was possible and most effective, despite the larger distance between the two electrodes.

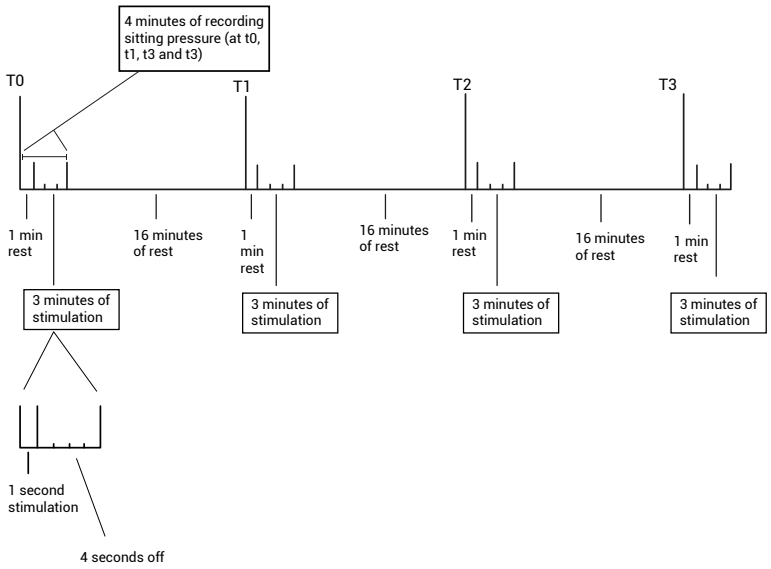

Figure 6.
Overview of 64 min of measurements, this is the same for both the stimulation of the g+h muscles and the exclusive stimulation of the g muscles.

Table 2 Differences (D) in pressure of the ITs and pressure gradient between stimulation and in rest, and for the last 3min of stimulation for

	t0 (Mean±s.d.)	t1 (Mean±s.d.)	t2 (Mean±s.d.)	t3 (Mean±s.d.)	Time (within protocol) P-value	Time * protocol P-value
D IT g	14.7±12.4	13.1±15.3	12.0±13.2	7.6±9.3	0.07	
g+h	44.0±28.1	42.0±28.5	35.1±24.2	28.5±17.7	0.01*	0.28
D Gradient g	6.5±7.7	5.9±12.4	4.4±10.8	4.3±8.9	0.65	
g+h	18.4±19.8	18.3±19.	13.9±18.0	8.2±19.8	0.10	0.41

Abbreviations: g, gluteal; g+h, gluteal and hamstring; IT, ischial tuberosity

A limitation that might have influenced this study were the ES-shorts. As this study only had one (washable) pair of ES shorts to work with. A few individuals, who met the inclusion criteria, were not to be able to participate, as the ES-shorts were too small. Unfortunately, the method of activating muscles as in this study is not suitable for persons with a flaccid paresis like in cauda equina syndrome. Intact sensibility might also sometimes be a problem, although in our study two participants had incomplete lesions with partially intact sensibility, but did not find the ES painful or even unpleasant.

ES-induced muscle activation might be a promising method in people with an SCI,[16] as it not only reduces pressure from ITs, but also may help to restore blood flow in compressed tissue, help to improve muscle condition and volume, and prevent PUs. Further study is needed to determine which pressure reduction is efficient and clinically relevant. The future aim is not to reduce pressure, but lower the incidence of PUs.

Conclusion

Both ES-induced activation of the g muscles only and g+h muscles provided significant reductions of IT pressure and pressure gradient. Activation of both the g+h muscles resulted in significantly better pressure reductions than activation of g muscles only, and the effect of the stimulation (pressure relief) was higher when stimulating both the g+h muscles, no matter what current was used. The pressure gradient only reduced significantly for the stimulation of both the g+h muscles. ES-induced muscle activation might be a promising method in people with an SCI, as it not only reduces pressure from ITs, but also may help to restore blood flow in compressed tissue, help to improve muscle condition and volume. Further research is needed to determine how much pressure reduction is sufficient to prevent PUs.

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5

Prolonged electrical-stimulation induced gluteal and hamstring muscle activation and sitting pressure in spinal cord injury: effect of duty cycle

Christof AJ Smit MD[1], Karin JA Legemate MSc[2], Anja de Koning MSc[2], Sonja de Groot PhD [1,3], Janneke M Stolwijk-Swuste MD, PhD[1], Thomas WJ Janssen PhD[1,2]

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ABSTRACT

Objective: To study and compare the effects of two duty cycles during 3 hours of electrical stimulation- induced gluteal and hamstring activation on interface pressure distribution in sitting individuals with a spinal cord injury (SCI), and to study the usability of a newly developed electrode garment.

Study Design: Ten individuals with SCI participated in this study, in which two electrical stimulation (ES) protocols with different duty cycles (1:1s vs. 1:4s on-off) were applied in counterbalanced order using a custom-made garment with built-in electrodes (ES-shorts).

Outcome variables: Interface pressure of the ischial tuberosities (IT pressure) and pressure gradient. A questionnaire was used to determine usability of the ES-shorts.

Results: In both protocols ES caused a significant decrease in average IT pressure compared to rest (=no ES); on average 35% for protocol 1:4 and 13% for protocol 1:1. The ES on-off duty cycle 1:4s showed less muscle fatigue. Participants scored the usability of the garment in general as satisfactory.

Conclusion: In this study the application of ES resulted in a significant decrease of IT pressure. The ES on- off duty cycle 1:4s is recommended because of the less fatiguing effect. ES of the hamstrings and gluteal muscles might be a promising method in preventing pressure ulcers, but further study is needed.

Introduction

Pressure ulcers (PUs) are the most prevalent secondary complications in individuals with a spinal cord injury (SCI). Throughout their life, up to 80% of the people with an SCI suffer from a PU[1,2,] leading to radical consequences such as decreased mobility and independence, delayed rehabilitation and exclusion from social activities[2,5]. This has a tremendous impact on the individual's physical and psychological condition[3,5]. The consequences also result in high costs for the community[3,4].

Prevention has focused on cushions to improve interface pressure distribution, and on pressure-relief movements[2,5]. Although interface pressure can be reduced with these methods, they are inadequate in completely preventing PUs[2,5]. Moreover, these are merely passive methods and do not activate the muscles, and therefore do not ameliorate intrinsic risk factors for developing PUs, such as muscle atrophy and decreased circulation.

Another potentially useful method for prevention of PUs is muscle activation by electrical stimulation (ES), which has been found to improve both interface pressure distribution and intrinsic risk factors, indicated by studies of Levine et al. [9,10,11,12] and others [3,4,5,19]. In previous studies [15,16], we demonstrated that surface ES of the gluteal muscles temporarily decreases interface pressure below the ischial tuberosities (IT's). Activation causes a change in muscle shape and muscle tone and leads the pressure away from the IT's in the direction of the knees. However, Van Londen et al.[15] included only a 30-minute stimulation protocol with self-adhesive

electrodes under the buttocks using a stimulator not suitable for daily life. Furthermore, no effects were studied for a longer period or using different protocols. It was unclear if muscle fatigue would occur after a longer period of stimulation, and if this would influence the pressure relieving effects of ES. In a subsequent study[16], we found that a 1-hour activation protocol of both hamstrings and gluteal muscles gives more pressure relief from the IT's than activation of the gluteal muscles only. In this study we discussed the desirable prolonged activation of these muscles.

Stimulation for longer period outside the laboratorium would be more like in daily life, and possibly generate muscle fatigue. In an interesting single-case study using implanted electrodes, Bogie et al.[5] described an on-off duty cycle of ES of 1:1 s in a 3-min period, with a 17-min interstimulation interval, approximating the frequency of weight shifting recommended for wheelchair users at risk of tissue breakdown[5,11,18]. This dynamic stimulation regime could be used for up to 10-hours a day while sitting in the wheelchair. However, this duty cycle has not been compared with other protocols and it is therefore not clear if this is the optimal stimulation-rest ratio.

In the present study we compared the same stimulation-rest interval (1:1) during the 3 minutes of ES with a different protocol (1:4). With this interval, activated muscles would be allowed to recover longer from contractions. We hypothesized that, as muscle contractions will be more effective over a longer period of time when fatigue does not occur, more rest might have more positive effects on pressure relief. In the present study, we used the previously used, specially developed ES-shorts with built-in electrodes connected to a portable stimulator. It has only been used in our previous study[15], but not in clinical practice. The aims of this study, therefore, were to determine:

1. The effect of 3 hours of ES-induced gluteal and hamstring activation on interface pressure distribution in sitting individuals with SCI (versus 30 min[15] and 60 min[16]).
2. The effects of duty cycle (1:1 vs 1:4) on interface pressure and subsequent muscle fatigue over time.
3. The usability of the electro-stimulation garment (ES shorts®).

Materials and Methods

Participants

Ten individuals with SCI having a complete or incomplete upper motor neuron lesion (ASIA A,B or C) aged between 18 and 70 years were recruited for this study, approved by the local medical ethics committee. Gluteal and hamstring muscles, skin under the buttocks, and spinal reflexes had to be intact, which was evaluated for all participants by one physician. Previous (plastic) surgery under the buttock area was no contra-indication for inclusion. Excluded were individuals with a flaccid paralysis and areflexia, a history of severe autonomic dysreflexia, current PUs under the ischial tuberosities or in the sacral region, severe cognitive or communicative disorders, intolerance for ES or any other contra-indication for ES. The participants provided written informed consent. Table 1 shows participants characteristics.

Table 1: Participants Characteristics

	N or Mean ± SD (range)
Participants (M/F)	10 (7/3)
Age (years)	40.6 ± 12.8 (26-58)
Lesion level	C3 - C8 (N=7) Th1-Th12 (N=3)
ASIA impairment classification	ASIA A: 6 ASIA B: 3 ASIA C: 1
Time since injury (months)	162 ± 99 (85-309)
Body mass (kg)	83.2 ± 15.4 (70-107)

Figure 1.

Table 2: Questionnaire on usability of the ES shorts

Question	Strongly agree	Agree	Agree nor disagree	disagree	Strongly disagree
1. I need help to put on the shorts	1	2	0	7	0
2. The shorts hinder me in daily activities	0	0	2	8	0
3. The stimulator (Neuropro) hinders me in daily activities	2	3	2	3	0
4. The short troubles me manipulating the indwelling or intermittent catheter	0	2	2	6	0
5. Electro-stimulation is painful	0	1	3	6	0
6. Of the two I preferred the 1:1 on-off duty cycle to the 1:4	0	0	0	8	2
7. I would wear the shorts in daily life, even all day, if proven effective in preventing pressure ulcers	2	8	0	0	0

Study design

The two 3-hour protocols with different duty cycles were performed on two separate days. in a counterbalanced order. Every participant had to put on the ES shorts (either individually or with assistance), and was allowed to wear normal pants over the ES shorts. In figure 1 these ES-shorts with electrical stimulator are shown. Each participant used his or her own wheelchair with daily-use cushion. The stimulation protocol lasted 3 hours, with interface pressure measurement sessions several times within the hour: during the last minute of both rest and stimulation periods. Between the measurement sessions, participants were allowed to perform normal daily activities in and around the rehabilitation centre. Finally, all participants completed a questionnaire on the usability of the ES-short, consisting of 7 questions (Table 2).

Electrical stimulation with the ES shorts

A stimulator (NeuroPro 8 channel, Axiobionics, Ann Arbor, MI, USA) connected with the custom-made ES Shorts® (Axiobionics, Axiobionics, Ann Arbor, MI, USA) was used to apply ES. These ES shorts are made of Lycra material containing flat embedded surface electrodes with built-in leads connected to the stimulator, to non-invasively activate the gluteal muscles and hamstrings. Electrodes align automatically over the gluteal and hamstring muscles as the ES shorts are put on, with one electrode positioned at the upper (proximal) part of the gluteal muscle above the sitting area, and one about halfway the hamstring loge, preventing the participant from sitting on electrodes or on the wires while wearing the shorts. The stimulator was attached around the subjects' waist with a strap. Ultrasound gel was applied over the electrodes and stimulation was delivered at standard 150 V, 50Hz bi-phasically to induce a tetanic contraction. The current amplitude resulting in the best pressure reduction was determined for each participant by increasing the amplitude in steps of 5-10mA to a maximum, without discomfort or excessive muscle contractions that would disturb normal

sitting. This amplitude was subsequently used for this participant for both protocols. Protocol 1:1 had a duty cycle of 1 s stimulation and
1s rest, while protocol 1:4 had a stimulation-rest ratio of 1 s on and 4 s off. The stimulation was applied for 3 min, followed by a 17-min rest period. This was repeated until 3 hours of stimulation and rest were completed.

Interface pressure measurements

Interface pressure distribution was measured using a pressure mapping device (Force sensitive array, FSA, Vista Medical, Winnipeg, Canada), a 2-mm thick soft flex mat of 42 x 42 cm consisting of 256 pressure sensors, placed between the cushion on the wheelchair and the buttocks of the participant. Before testing, it was calibrated between 0 and 200 mmHg according to the systems' calibration protocol.

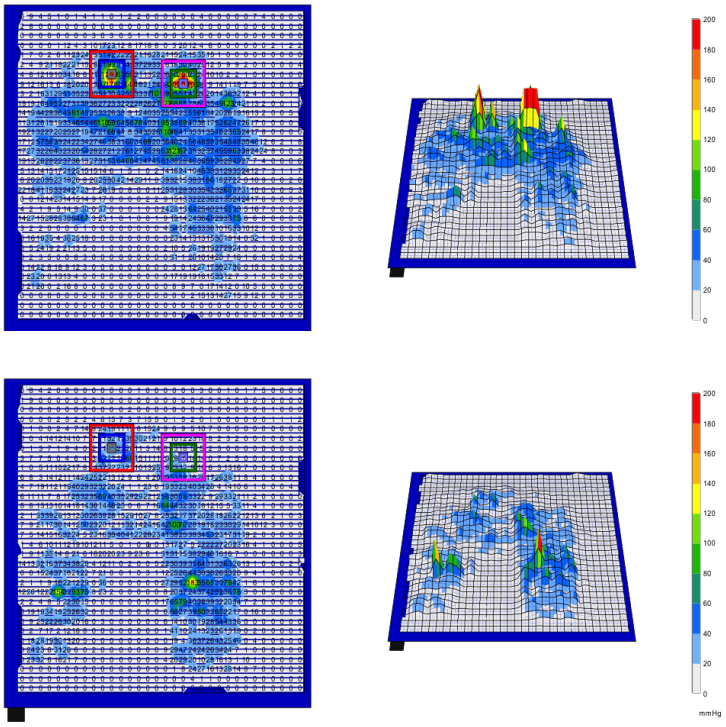

Figure 2.

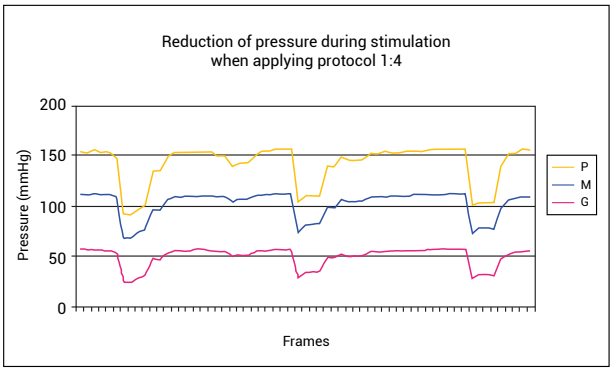

Figure 3.

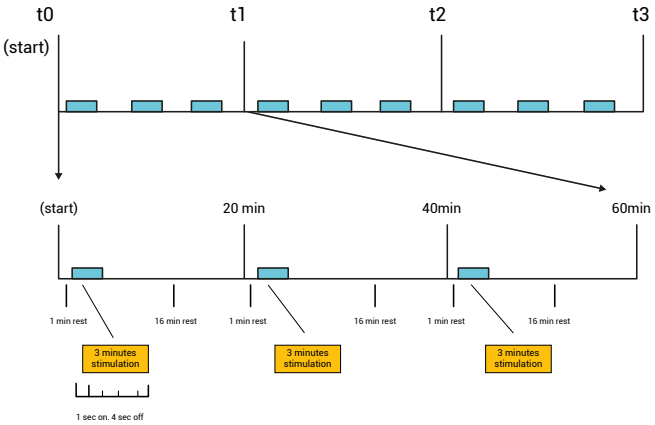

Figure 4.

The participant had to sit in a 'normal position'; feet on the footrests, arms on the armrests (if any) or on participants lap, and the lower back against the backrest of the wheelchair. The individual had to sit in his or her wheelchair on the FSA for 5 minutes to allow the cushion to adapt to the participant's buttocks. Subsequently, the protocol was started and outcome variables were obtained during stimulation, and in the last minute of rest (just prior to stimulation). The two IT areas were defined as the 3x3 sensors with the highest pressure values. The values of the 9 sensors were averaged to result in the IT pressure for left and right IT area. The pressure gradient was calculated by distracting the mean pressure from

the (average) values of the 9 sensors in the tuber area and the 16 surrounding sensor values (figures 2 and 3). The pressure gradient may indicate shear forces[2,16]. Higher shear forces cause a higher risk on tissue damage and PUs[1,2, 6,10].
Pressure values were recorded during the 3 minutes of stimulation and during the last minute of the preceding rest. This produced four Force Sensitive Array (FSA) recordings per hour, namely t0 (before start), t1, t2 and t3. In figure 4 measurements within one hour are shown.

Data analysis

IT pressure and pressure gradient, collected with the FSA, were calculated by averaging the values for right and left buttock. The acute effects of stimulation were investigated by calculating delta IT pressure, subtracting the lowest pressure value of all stimulation moments during 3 minutes of stimulation from the average pressure values at rest at the different moments in time. Delta pressure gradient was calculated subtracting the mean values of the pressure gradient with ES from average pressure values at rest. This resulted in variables Δ IT Pressure and Δ Gradient at t0, t1, t2 and t3 for both protocols. To establish whether muscle fatigue had occurred, interface pressure during the last 3 stimulations of the 3-minute stimulation period at T3 was compared with pressure values in rest at T0. When fatigue occurs contractions will be less forceful, which is expected to result in a diminished Δ IT pressure and Δ Gradient. Differences were also calculated at t0, t1, t2 and t3 for both protocols.

Statistical analysis

SPSS for Windows software (version 16.0, Chicago, Il, USA) was used to analyze the data. All results were described as mean ± standard deviation (SD). Repeated measures ANOVA were used to analyse data (IT pressure and pressure gradient) within the protocol (1:1 and 1:4). A 2 x 4 within-within general linear model ANOVA with repeated measures (2 protocols x 4 moments in time) was used to compare data of the two protocols over time. Differences with a p-value ≤ 0.05 were considered significant. Descriptive statistics were performed to analyse the questionnaires.

Results

Effects of 3 hours ES on interface pressure

All participants were stimulated with ES ranging from 70mA to a maximum of 115mA. Both protocols resulted in an acute significant decrease of pressure during stimulation compared to rest (non ES) for all measured values; i.e.: IT pressure and Pressure gradient (Table 3). For example IT pressure decrease at T0: from 106 mmHg to 37.2 mmHg (39%) (protocol 1:1) and from 103 mmHg to 31.2 mmHg (32%) (protocol 1:4). Muscles fatigued only after protocol 1:1 as delta IT pressure tended to decrease over time (within protocol p=0.06).

Differences between protocols

IT pressure and pressure gradient during stimulation compared with rest were not significantly different between protocols (Time within protocol), although there was a tendency of larger reductions for 1:4 than for 1:1. Over time protocol 1:4 had significantly more effect than protocol 1:1 for delta IT pressure (p= 0.04;Table 3). While effects reduced in the 1:1 protocol (i.e. less pressure reduction), the effects remained stable in the 1:4 protocol (fig. 5). This was not the case for delta gradient (p=0.33) (Time * protocol). Fatigue occurred after the application of protocol 1:1 more than of 1:4 as in the last 3 minutes of stimulation, there is a significant difference between protocols for pressure reduction (p<0.001) over time.

Usability of the ES shorts

All participants completed the questionnaire after the measurements (Table 2). Three of the 10 participants were not able to put on the ES-shorts without help; their lesion was at level C6 or higher. None of the participants found the ES-shorts interfering with daily activities (such as riding the wheelchair), but the stimulator did hinder 5 of the participants in daily activities. Six participants had an indwelling catheter and two of them perceived the shorts to hinder the working of the catheter, another two indicated that the shorts were not comfortable in combination with their catheter. Only one participant mentioned the stimulation as painful. Nobody had trouble to sustain the 3-minute stimulation periods. All participants reported they experienced protocol 1:4 as the more comfortable of the two. Finally, if the ES-shorts were found helpful in preventing PUs, all the participants stated they would be willing to use the shorts all day long in daily life.

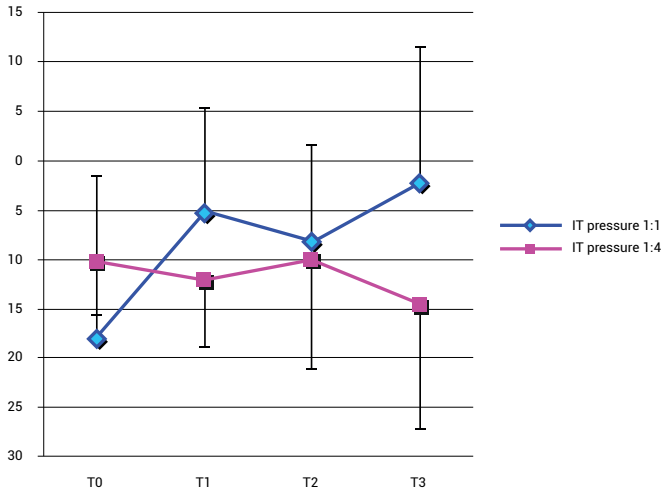

Figure 5.

Table 3: Differences (Δ; Mean ± sd) in pressure of the ischial tuberosities (ITs) and pressure gradient between (ES induced) activation and in rest at the end of blocks T0, T1, T2 and T3, and for the very last 3 minutes of ES induced activation at T3 compared with rest at T0; for both protocol 1:1and 1:4.

		T0	T1	T2	T3	Time (within protocol) p-value	Time * Protocol p-value
Δ IT pressure	1:1	-37.2 ± 44.2	-12.7 ± 13.1	-16.1 ± 14.6	-9.0 ± 19.2	0.06*	0.04*
	1:4	-31.2 ± 44.2	-33.2 ± 19.8	-29.5 ± 18.2	-36.4 ± 20.5	0.62	
Δ Gradient	1:1	-18.8 ± 33.9	-7.1 ± 9.3	-8.2 ± 10.0	-5.7 ± 11.2	0.34	0.33
	1:4	-16.1 ± 11.2	-22.5 ±19.7	-14.2 ± 18.8	-18.3 ±17.9	0.53	
Δ IT pressure 3min	1:1	-18.1± 16.5	-5.4 ± 10.7	-8.3 ± 9.9	-2.4 ± 13.9	0.02*	0.00*
	1:4	-10.3 ± 5.4	-12.1 ± 6.8	-10.2 ± 11.0	-14.7 ± 12.5	0.34	
Δ Gradient 3min	1:1	-4.1 ± 8.8	-3.0 ± 6.1	-4.0 ± 5.6	-2.3 ± 7.1	0.86	0.87
	1:4	-3.1 ± 7.1	-5.8 ± 20.5	-3.3 ± 11.5	-5.1 ± 10.2	0.93	

Table 2: Questionnaire on usability of the ES shorts

Question	Strongly agree	Agree	Agree nor disagree	Disagree	Strongly disagree
1. I need help to put on the shorts	1	2	0	7	0
2. The shorts hinder me in daily activities	0	0	2	8	0
3. The stimulator (Neuropro) hinders me in daily activities	2	3	2	3	0
4. The short troubles me manipulating the indwelling or intermittent catheter	0	2	2	6	0
5. Electro-stimulation is painful	0	1	3	6	0
6. Of the two I preferred the 1:1 on-off duty cycle to the 1:4	0	0	0	8	2
7. I would wear the shorts in daily life, even all day, if proven effective in preventing pressure ulcers	2	8	0	0	0

Discussion

The purpose of this study was to investigate the effect of surface ES on the interface pressure distribution in sitting individuals with an SCI tested over a 3 hour period. This is a longer period than in previous studies and more comparable with a daily life situation[15,16]. The results in this study showed clear reductions in IT pressure and pressure gradient of the buttocks during ES, which is in line with previous studies[2,5,12,15,16,18,19]. During ES an increase in pressure was seen in the area of the upper legs, as the pressure was relocated from the IT's to the front of the sitting surface. This (desirable) relocation did not give any skin problems there, as there are no bony prominences at the hamstring site near the knees.

Bogie et al.[5] described an on-off duty cycle of ES of 1:1 s in a 3-min period, with a 17-min interstimulation interval, approximating the frequency of weight shifting recommended for wheelchair users at risk of tissue breakdown [5,11,18]. This duty cycle has not been compared with other protocols and it is therefore not clear if this is the optimal stimulation-rest ratio. We have compared the same stimulation-rest interval (1:1) during the 3 minutes of ES with a different protocol (1:4). Comparison of these 2 ES on-off duty cycle protocols revealed that protocol 1:4 had preferable effects over protocol 1:1. We showed that over 3 hours of stimulation in this protocol (1:4) participants' gluteal and hamstring muscles kept contracting without marked muscle fatigue. This suggests that probably perfusion, as well as oxygenation, was sufficient during the 3 hours of testing. This is also found in studies of Gerrits et al.[8], and Janssen et al.[6,7] showing the improvement of blood flow and oxygenation in stimulated paralysed muscles of people with SCI.

The decline of the pressure relief effect over time in protocol 1:1 is likely caused by less forceful contractions due to muscle fatigue after repetitive activation. We hypothesize that ES-induced training of these muscles will have a positive effect on fatigue. Muscles in good condition will be better perfused and oxygenated, and likely continue to contract after prolonged activation. We don't know whether an other duty cycle (for example on–off ratio 1:6) and or rest period (for example shorter than 17 min) will have even more preferable effects on pressure relief versus fatigue. How much recovery time muscles need for continues activation after stimulation? In literature no studies were found describing effects of ES training on fatigue or sitting pressure in people with SCI or other diagnose groups. This needs further investigation. In addition, comparing effects of both protocols, all participants reported in the questionnaire on usability they experienced protocol 1:4 more comfortable. In conclusion protocol 1:4 overall objectively and subjectively had preferable effects over 1:1.

This method is non-invasive, the costs are relatively low and electrodes are fabricated within the ES- shorts, and therefore do not have to be placed repeatedly. The used stimulator is relatively small and easily portable, but hinders 5 of 10 participants. Challenge for the future is to improve this stimulator. Most importantly by reducing the size and its weight. Also, this new method has a major advantage over systems such as the dynamic seating systems[18,19], in the sense that it can be used independently from the daily use wheelchair. The ES system "travels" with the person without the need to make any changes or arrangements. It can be used while

sitting on the couch, while sitting on the plane during a 10-hr flight, while sitting in a sports wheelchair, etc. In addition to that advantage, no lifting is needed, which reduces the load on the shoulders and with this the risk of shoulder and arm injuries[14]. Moreover, the ES shorts are worn under the regular clothes[20]. Although some participants reported practical problems, such as applying the ultrasound gel or handling the stimulator, none of the subjects reported any relevant side effects while receiving ES wearing the shorts. The shorts were found to be feasible for the application of ES in daily life situations. Participants all stated they would wear the short with the stimulator in daily life, even all day long, if it helped them to prevent PUs.

For preventing PUs it will be necessary to determine which reduction of pressure is clinically relevant and therefore how often the ES shorts should be worn to prevent PUs. Circulation and oxygenation measurements in the gluteal and hamstring area are also interesting to deter effects of surface ES on tissue deeper under the stimulated surface. Future research also has to reveal the possible additional effects of surface ES on reduction of muscle atrophy. Levine et al.[9,10,11,12] already showed that tissue shape changed and muscle hypertrophy occurred after electrical muscle stimulation.

Unfortunately, the method of activating muscles used in this study is not suitable for persons with a flaccid paresis such as in cauda equine syndrome. Also intact sensibility might sometimes be a problem, although in our study the 2 participants who had incomplete lesions with partially intact sensibility, did not perceive the ES painful or even unpleasant. There was 1 participant who did find the stimulation unpleasant. She had a Asia A- lesion but with a zone of partial (preserved) innervation, causing painful sensations above a certain stimulation level. For further research we recommend to provide a customised ES-short for each individual participant. This is important as compliance wearing the short is of course of vital importance. Future research has to reveal long-term effects of ES on circulation and oxygenation and which pressure reduction actually decreases the incidence of PUs. The usability of the ES-shorts can also be improved, especially with regard to the ultrasound gel. Results so far are promising and suggest that surface ES might help preventing PUs in sitting individuals with SCI.

Conclusion

ES applied to the gluteal and hamstring muscles in a custom-made electrode garment with built-in electrodes gives significant pressure relief of the ischial tuberosities even after 3 hours of activation in individuals with an SCI. ES on- off stimulation ratio 1:4s versus 1:1s gave better results in pressure relief during a 3 hours protocol, without marked muscle fatigue. Participants scored the usability of the ES shorts in general as satisfactory and all stated they would daily wear them should they help prevent PUs.

Conflict of interest:

The authors declare no conflict of interest.

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6

Gluteal blood flow and oxygenation during electrical stimulation induced muscle activation versus pressure relief movements in wheelchair users with a spinal cord injury

Christof AJ Smit MD[1], Maremka Zwinkels MSc[2], Tim van Dijk MSc[2], Sonja de Groot PhD [1,3], Janneke M Stolwijk-Swuste MD, PhD[1], Thomas WJ Janssen PhD[1,2]

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ABSTRACT

Background: Prolonged high ischial tuberosities pressure (IT pressure), decreased regional blood flow (BF), and oxygenation (%SO2), are risk factors for developing pressure ulcers (PUs) in spinal cord injury (SCI). Electrical stimulation (ES) induced gluteal and hamstring muscle activation may improve pressure distribution by changing the buttocks' shape while sitting and increase BF and %SO2.

Objective: to compare acute effects of ES-induced gluteal and hamstring muscle activation with pressure relief movements (PRM's) on IT pressure, BF and %SO2.

Participants and methods: 12 men with SCI performed PRM's: push up, bending forward, leaning sideward, and received surface ES (87±19 mA) to the gluteal and hamstring muscles while sitting in their wheelchair. Ischial tuberosities pressure was measured using a pressure mapping system; (sub) cutaneous BF and %SO2 by reflection spectroscopy and laser Doppler.

Results: Compared to rest (156±26 mmHg), IT pressure was significantly lower during all conditions (push up 19±44; bending forward 56±33, leaning sideward 44±38, ES 67±45 mmHg). For the whole group, all PRM's significantly augmented BF (+39-96%) and %SO2 (+6.0-7.9 %-point), while ES-induced muscle activation did only for peak BF. 63% of the participants showed an increased BF (average 52%) with ES.

Conclusion: PRM's acutely reduced IT pressure and improved oxygenation and BF in SCI. The currently used ES-method cannot replace the PRM's, but may be used additionally. ES-induced muscle activation is not as effective in acute pressure relief, but the frequency of stimulation is much higher than the performance of PRM's, and can therefore be more effective in the long term.

Introduction

Pressure ulcers (PUs) are the most prevalent secondary complications in individuals with a spinal cord injury (SCI). Throughout their life, up to 80% of the people with an SCI suffer from a PU[1,2], leading to radical consequences such as decreased mobility and independence, delayed rehabilitation, exclusion from social activities[2,5,] and a tremendous impact on the individual's physical condition[3,5]. The consequences also result in high costs for the community[3,4].

Shifting posture regularly, on average eight times an hour, prevents healthy individuals from developing PUs, as subcutaneous oxygenation increases with each posture adjustment[4]. Preventive measures like pressure relief movements (PRM's) and pressure distributing cushions are passive methods and not adequate enough, as PUs still occur. Besides, although PRM's like bending forward, leaning sideward and/or lifting improves blood circulation in compromised tissue, they require good upper-limb strength and generate high pressure on the gleno-humeral joint, possibly resulting in shoulder injuries[6]. In addition, the person must be well motivated to continue lifting for eight times every hour. Furthermore, tissue properties do not improve.

Recent research showed that electrical stimulation (ES) of the tuber area in persons with an SCI had a direct positive effect on interface pressure distribution, blood flow and muscle size[8-12]. Levine et al[9-10] used surface ES in the gluteal muscles of individuals with SCI and found a changed buttock tissue shape[9] and increased muscle blood flow[10]. Ferguson et al[8] stimulated the quadriceps muscles and found a decrease in interface pressure as well. Smit et al[14] found that ES-induced gluteal and hamstring muscles activation reduces IT pressure and in a 3-hour stimulation period with a 1:4 seconds on-off duty cycle does not cause muscle fatigue. Bogie et al1 examined the long-term effects of ES, using implanted electrodes in the gluteal muscles to electrically stimulate the muscles. This long-term study found increased gluteal muscle thickness and increased blood flow, together with a decrease in interface pressure. A more practical intervention was recently introduced in a study by Smit et al[14], describing the effects of a non-invasive ES method on interface pressure distribution, using electro stimulation-shorts (ES-shorts).

The positive effect of ES on interface pressure as well as the positive effect of shifting posture on oxygenation have been demonstrated[18,19]. However, there is no extensive literature describing the effect of ES on ischial oxygenation nor has the effect of ES been compared to the effect of PRM's or the relationship between IT pressure and oxygenation and BF been described.

The present study therefore aimed to answer the following questions:

1. What are the acute effects of ES-induced gluteal and hamstring muscle activation on IT pressure, BF, and oxygenation, compared with three pressure relief movements?
2. Is there a relationship between IT (sitting) pressure and oxygenation or blood flow?

We hypothesized that ES and pressure relief movements would both decrease IT pressure and increase BF and oxygenation (%SO2) and that a negative relationship exists between interface pressure and oxygenation or BF.

Materials and methods

Participants

Twelve men with SCI, having a complete or incomplete upper motor neuron lesion (ASIA A or B), aged between 18 and 60 years were recruited for this study, which was approved by the local medical ethics committee. Gluteal and hamstring muscles, skin under the buttocks, and spinal reflexes had to be intact, which was evaluated for all participants by one physician. Excluded were individuals with a flaccid paralysis and areflexia, a history of severe autonomic dysreflexia, current IT pressure ulcers, severe cognitive or communicative disorders, intolerance for ES or any other contra-indication for ES. Participants provided written informed consent. Participants' characteristics in tables 1 and 2.

Table 1. Participants Group characteristics.

	Mean ± SD (range)
Participants (M/F)	12 (12/0)
Age (years)	38.1 ± 12.8 (26-52)
Lesion level	C3 - C8 (N=7) Th1-Th12 (N=5)
AIS impairment classification	ASIA A: 9 ASIA B: 3
Time since injury (months)	173 ± 93 (85-503)
Body mass (kg)	82.2 ± 15.0 (64-107)

Table 2. Participants individual characteristics.

Participant	Gender M/F	Age	Lesion Level	AIS Score	Time since injury (years)
1	M	41	C5	B	8,1
2	M	32	C6	B	12,0
3	M	28	C7	A	7,2
4	M	50	C8	B	9,9
5	M	38	C6	A	10,0
6	M	52	C6	A	16,8
7	M	37	C5	A	13,2
8	M	28	T11	A	18,8
9	M	41	T10	A	41,9
10	M	48	C7	A	19,6
11	M	36	C4	A	15,8
12	M	26	T8	A	7,8

Study design

This study was performed in a Rehabilitation Research Centre. Measurements lasted about 4 hours per participant. Each participant used his or her own wheelchair with daily-use cushion, most of them where aircushions (n= 10; ROHO, Vicair or Starlock), some used gel (n=2; Jay2), with a force sensitive array on top. Before measurements started a 1.0 x 1.5 cm probe, 0.1 cm thick, was attached under the left ischial tuberosity with surgical tape, while the participant was sitting in his chair and performed a bend over to the right site. After attachment of the probe, it was then connected to the oxygenation device. Participants were then asked to perform PRM's in a counterbalanced order: bending forward, leaning sideward (to the right side to release the probe), and push up, for as long as possible, with a maximum of 2 minutes (figure 1). Before each measurement the participant had to sit and rest for five minutes. Every measurement started with 30 seconds of rest to gain a baseline value of interface pressure and oxygenation.

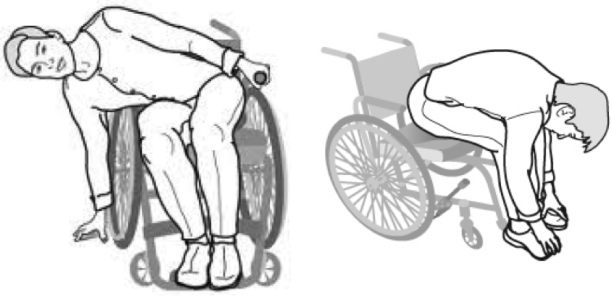

Figure 1. Exaples of Pressure Relief Movements (PRMs). Leaning sideward and bending forward.

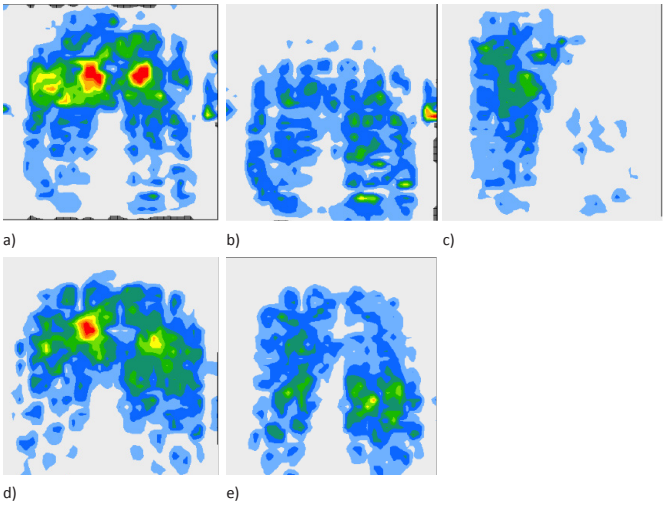

Figure 2.
Raw interface pressure data of the mFLEX during resting (a), bending forward (b), leaning sideward (c), a stimulation period without (d) and with (e) ES induced muscle contraction. Push up is left out because it showed no interface pressure. red color indicates high pressure, and blue low. First 30 secondes are rest.

Then, after a 30 min rest period, in which self-adhesive surface electrodes, 2 on each leg, were applied, both gluteal and hamstring muscles were activated by electrical stimulation. Outcome variables: IT pressure, ischial oxygenation and blood flow were measured in rest, during all pressure relief conditions and during ES-induced gluteal and hamstring muscles activation.

Interface pressure measurement

Interface pressure distribution was measured using a pressure mapping device (Force sensitive array, mFlex®, Vista Medical Europe, Venlo, the Netherlands): a 2-mm thick soft flex mat of 42 x 42 cm consisting of 256 pressure sensors, placed between the cushion on the wheelchair and the buttocks of the participant. Before testing, it was calibrated between 0 and 200 mmHg according to the systems' calibration protocol.

The participant had to sit in a 'normal position'; feet on the footrests, arms on the armrests (if any) or on participant's lap, and the lower back against the backrest of the wheelchair. Before the protocol was started the individual had to sit in his wheelchair on the FSA for 5 minutes to allow the cushion to adapt to the participant's buttocks. Pressure data were recorded continuously (one per second). Both IT areas were defined as the 3x3 sensors with the highest pressure values. Mean pressure values of both IT areas were used for statistical analysis. See figure 2.

Oxygenation and circulation

Oxygenation data were obtained using Oxygen To See device (O2C, LEA Medizintechnik GmbH, Giessen, Germany). The rigid O2C probe is able to measure the oxygen saturation of hemoglobin (%SO2) at the venous end of the capillaries, the quantity of hemoglobin in the micro-blood vessels and the velocity of flow of the blood in the microcirculation, by using a non-invasive combination of reflection spectroscopy and the laser Doppler technique. According to the manufacturer's manual, O2C reliably measures to

a depth of approximately 10 mm. %SO2 is used as an indicative measure for oxygenation in muscle tissue[4]. From the moment that %SO2 reached a constant value the mean %SO2, and mean BF and peak BF was calculated. To correlate oxygenation and blood flow with interface pressure data, both measurements were performed simultaneously.

Electrical stimulation

A stimulator (NeuroPro 8 channel, Axiobionics, Ann Arbor, MI, USA) was connected with 2 surface electrodes per leg positioned at the upper (proximal) part of the gluteal muscle above the sitting area, and one about halfway the hamstring area, preventing the participant from sitting on electrodes or on the wires while being stimulated (figure 3). ES was delivered at standard 150 V, with 50Hz (bi-phasically) to induce a (visible) tetanic contraction. Prior to stimulation the current amplitude resulting in the best pressure reduction was determined for each participant by increasing the amplitude in steps of 5-10mA to a maximum, without discomfort or excessive muscle contractions disturbing normal sitting. This amplitude was applied with a duty cycle of 1 s stimulation and 4 s rest for 3 minutes. We did not train the participants with ES.

Figure 3.
NeuroPro 8-channel electro stimulator, Axiobionics, Ann Arbor, MI, USA, with self-adhesive surface electrodes

Statistical analysis

Values were described by mean values ± standard deviation (SD). A repeated measures ANOVA was performed to compare both oxygenation, blood flow and IT pressure between all conditions (rest, pressure relief movements and ES). A post-hoc test was executed when a significant difference was found ($\alpha<0.05$) to indicate which conditions differed from each other. The relationship between oxygenation and IT pressure and between (peak) blood flow and IT pressure was calculated by correlating mean changes between rest and condition (Pearson correlation coefficient). Statistical analysis was performed using SPSS for Windows 17.0 (Chicago, Illinois, USA).

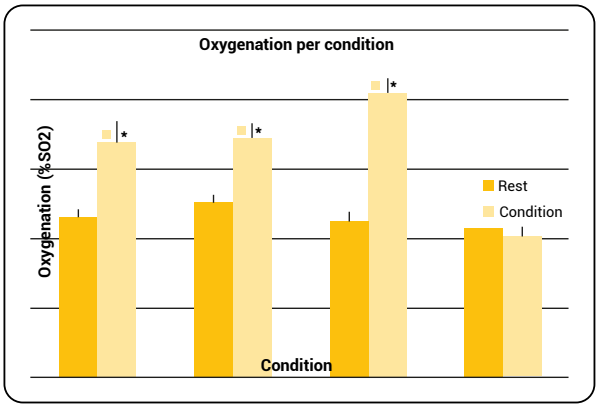

Figure 4.
The mean IT oxygenation per condition compared with rest just before the action. * Significant increase in oxygenation compared with rest

Results

During this study, none of the participants developed skin problems due to the rigid O2C probe, or complaints of autonomic dysreflexia during PRM's, nor during ES induced gluteal- and hamstring muscles activation. The amplitude of ES varied between 55mA and 125mA, with an average of 87mA (±18.5).

IT pressure

Compared to rest (156±26 mmHg), IT pressure was significantly lower during all conditions (push up 19±44 mmHg ($p<0.001$); bending forward 56±33 mmHg ($p<0.001$), leaning sideward 44±38 mmHg ($p<0.001$)). ES-induced gluteal and hamstring muscles activation reduced IT pressure to 67±45 mmHg ($p=0.03$). The post-hoc test indicated no significant difference between PRM and ES conditions.

Oxygenation

Due to technical problems with the O2C only the data of 9 participants were reliable.

Bending forward ($p=0.01$), leaning sideward ($p=0.01$) and push up ($p=0.01$) significantly increased mean oxygenation compared to rest, while ES did not ($p=0.57$). No significant difference was found between the different passive PRM's (figure 4). A weak and non-significant correlation was found between mean oxygenation change and (mean) IT pressure change for the PRM's, while it was strong and significantly correlated for ES ($r=0.7$)(Table 3).

Table 3. Correlations between changes in interface pressure and oxygenation and interface pressure and blood flow. * Significant correlation at $p<0.05$

Correlation	oxygenation - interface pressure		blood flow – interface pressure	
	r	p	r	p
Forward bending	0.16	0.69	0.03	0.94
Leaning sideward	-0.10	0.98	-0.51	0.16
Push up	-0.26	0.62	0.36	0.49
Electrical Stimulation	0.70	0.04*	0.54	0.14

Table 4. Correlation of Peak blood flow between different conditions.
* Significant correlation at $p<0.05$

Peak Blood Flow		
Correlation	Mean (±SD)	p-value
Rest- ES	66.4 (59.8)	0.007
Rest- Bending Forward	172.3 (153.6)	0.006
ES- Bending Forward	105.9 (177.3)	0.092

Blood flow

Compared to rest, bending forward (p=0.02), leaning sideward (p=0.03) and push up (p=0.02) increased the blood flow significantly. However, ES did not cause a significant change (p=0.75) in mean BF. There was a significant difference in peak BF for ES (p=0.007), and for bending forward (p=0.006) compared to rest (table 4). Change in blood flow was significantly lower for ES than all PRMs and a significant larger increase was found for push up compared to leaning sideward, but not compared to bending forward (figure 5). A clear correlation was found between blood flow change and mean interface pressure change for all conditions, although it was only moderate for push up and for ES (table 3). However, figure 6 indicates a certain relationship over time for two participants, as the blood flow increases directly after applying ES while the interface pressure decreases.

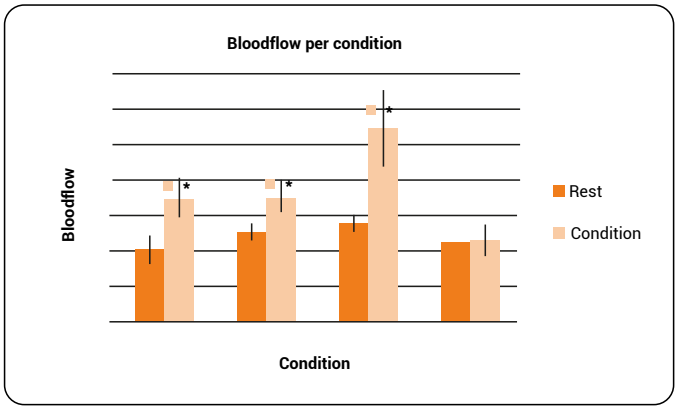

Figure 5.
The mean blood flow under the tuber per condition, compared with rest just before the action. * Significant increase.

Discussion

The present study showed that PRM's induced significant acute reductions in interface pressure, and directly improved (sub)cutaneous oxygenation and blood flow in sitting wheelchair users with SCI. We hypothesized that ES-induced muscle activation would also increase blood flow and oxygenation; however, this study does not support that. The relation between IT pressure and circulation showed that blood flow is influenced by IT pressure in some participants. ES increased blood flow and oxygenation in 8 of 12 participants (63%)(figure 6), however, ES did not change mean blood flow or oxygenation when analyzed over the whole group (figure 5). ES and bending forward significantly increased Peak BF. For ES this can be explained by the 1 second induced muscle contraction causing a peak in blood flow, as well as a reduction of blood flow when the muscle relaxes again. Average values of blood flow are lower of course, but this significant difference in peak blood flow supports the finding in several studies that (prolonged) ES-induced muscles activation induces blood flow.

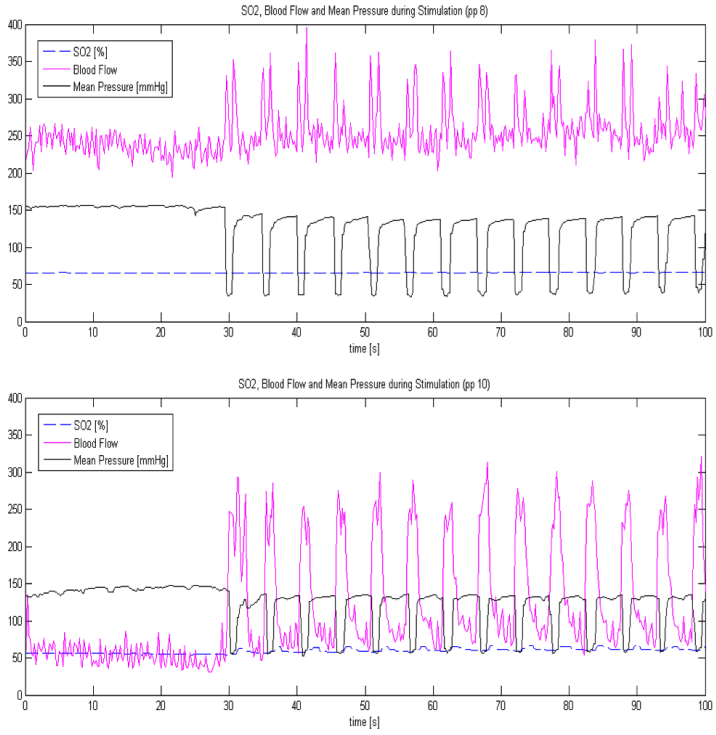

Figure 6.
Blood flow, oxygenation and mean pressure during rest and stimulation of 2 participants over time. ES started after 30 s of rest. Oxygenation is in %SO2, mean pressure is in mmHg, and blood flow is arbitrary so no unit is reported here.

Muscle activation did reduce IT pressure in 8 participants, but the reduction may not have been adequate to increase mean blood flow and oxygenation. In all the 4 participants, where no reduction of IT pressure was found due to muscle activation, more muscle atrophy was seen than in the other 8, possibly causing the different effect on IT pressure reduction due to (less absolute) muscle activation. In future study inducing stronger contractions with more current might be necessary, as well increasing the number of participants, for more statistical power.

Olive et al16 stated that impaired or altered blood flow to affected muscles during exercise or ES-induced contractions have been reported in SCI subjects and may contribute to increased muscle fatigue[15,16,17].

Crespo Ruiz et al[18], described the physiological training effects: muscles will enlarge, become stronger, and circulation will improve. ES-induced muscle activation with tetanic contractions allows mechanically unrestricted blood flow and may lead to less fatigue as a result of changes in the tissue. Therefore it is interesting, not only to induce stronger contractions, but also enlarge the period of applying ES on gluteal and hamstring muscles. In the present study peak blood flow is significantly increased by ES-induced muscle activation, and although acute effects of ES-induced muscle activation, may not be as good as those from PRM's, prolonged ES-induced activation and training of the gluteal and hamstring muscles may in contrast induce positive structural changes in muscle tissue, circulation, and IT pressure distribution.

Furthermore, ES-induced muscle activation in SCI results in improved cardio-respiratory capacity, such as maximal aerobic power, peak oxygen consumption, forced expiratory flow, and forced vital capacity[18,19]. This may exert a decisive influence on the capacity to transport oxygen in the areas most affected by disuse resulting from the SCI itself. This is especially important when prolonged treatment is required, for example, in an attempt to prevent pressure ulcers[13]. However, further studies are needed to confirm these findings.

There were two study limitations. One concerns the O2C device, which is sensitive to disturbing influences. Although we followed the manufacturer's recommendations and carried out all measurements in the same room, with the same environmental factors, reduced the amount of surrounding light and kept temperature at a more or less constant level, the results can be influenced by the amount of light from the surrounding area and also by the temperature of the room. In 3 participants data were unreliable as the probe recorded too much surrounding light. The other limitation concerns the interface pressure mapping, which does not provide information about load at deep tissue. Solis et al. found that superficial ES delivered every 10 min is sufficient to reduce greatly the extent of damage in deep tissue exposed to constant external pressure20. When external load decreases, internal load decreases as a result as well, but more insight in the relationship between IT pressure and deep tissue injury is needed to provide information on the validity of external interface pressure measurements.

One of the clinical implications of this study relates to the effects of the different PRM's. Push-ups require good upper-limb strength, and generate undesirable high pressure on the gleno-humeral joint, often resulting in shoulder injuries, where bending forward is easy to perform and not as heavy loading the shoulders. Our results confirm that bending forward and side

wards, is as least as sufficient as a complete push up, for the recovery of gluteal blood flow and oxygenation. In clinical (rehabilitation) practice stronger evidence from present study now confirms that no longer push-ups should be advised, but rather bend forward to release IT pressure, and improve gluteal blood flow and oxygenation.

Conclusion

Both pressure relief movements and ES-induced muscle activation induced significant acute reductions in interface pressure. PRM's directly improved (sub)cutaneous oxygenation, peak and mean blood flow significantly, while ES-induced contractions increased peak blood flow, and blood flow and oxygenation in some participants. Bending forward, leaning side wards and push-ups showed similar increases in IT blood flow and oxygenation in SCI. The currently used (ES-) method cannot replace the PRM's, but may be used additionally. ES-induced muscle activation is not as effective in acute pressure relief, but the frequency of muscle activation stimulation is much higher than the performance of PRM's, and could therefore be more effective in the long term.

Conflict of interest:

The authors declare no conflict of interest.

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Tables 1 to 4

Table 1. Participants Group characteristics.

	Mean ± SD (range)
Participants (M/F)	12 (12/0)
Age (years)	38.1 ± 12.8 (26-52)
Lesion level	C3 - C8 (N=7) Th1-Th12 (N=5)
AIS impairment classification	ASIA A: 9 ASIA B: 3
Time since injury (months)	173 ± 93 (85-503)
Body mass (kg)	82.2 ± 15.0 (64-107)

Table 2. Participants individual characteristics.

Participant	Gender M/F	Age	Lesion Level	AIS Score	Time since injury (years)
1	M	41	C5	B	8,1
2	M	32	C6	B	12,0
3	M	28	C7	A	7,2
4	M	50	C8	B	9,9
5	M	38	C6	A	10,0
6	M	52	C6	A	16,8
7	M	37	C5	A	13,2
8	M	28	T11	A	18,8
9	M	41	T10	A	41,9
10	M	48	C7	A	19,6
11	M	36	C4	A	15,8
12	M	26	T8	A	7,8

Table 3. Correlations between changes in interface pressure and oxygenation and interface pressure and blood flow.
* Significant correlation at p<0.05

Correlation	oxygenation - interface pressure		blood flow – interface pressure	
	r	p	r	p
Forward bending	0.16	0.69	0.03	0.94
Leaning sideward	-0.10	0.98	-0.51	0.16
Push up	-0.26	0.62	0.36	0.49
Electrical Stimulation	0.70	0.04*	0.54	0.14

Table 4. Correlation of Peak blood flow between different conditions.
* Significant correlation at p<0.05

Peak Blood Flow		
Correlation	Mean (±SD)	p-value
Rest- ES	66.4 (59.8)	0.007
Rest- Bending Forward	172.3 (153.6)	0.006
ES- Bending Forward	105.9 (177.3)	0.092

7

Feasibility of overnight electrical stimulation-induced muscle activation in people with a spinal cord injury

Christof AJ Smit, Frank Berenpas MSc, Sonja de Groot, Janneke M Stolwijk-Swuste, Thomas WJ Janssen

Submitted

ABSTRACT

We investigated whether overnight ES is a feasible method to activate gluteal, quadriceps and hamstrings muscles in a two-week experiment. Electrical stimulation (ES) induced muscle contractions have proven positive effects on risk factors for developing pressure ulcers in people with a spinal cord injury (SCI). Therefore prolonged overnight ES induced muscle activation is interesting, but has never been studied. Objective of this study was to study muscle fatigue and feasibility of ES induced leg muscle activation. In eight participants with motor complete SCI gluteal, hamstrings and quadriceps muscles were activated with a 2-weeks overnight stimulation protocol, 8 hours per night, using specially developed ES-shorts. Muscle fatigue was determined with a muscle contraction sensor. Questionnaires on sleep quality (SQ) and the ES-shorts usability were taken. Results show that after 8 hours of activation muscles still contracted, although fatigue occurred and mean contraction size was lower at the end of a cycle (p=0.03). SQ (0-100) after intervention was 75, and 66 after 4 weeks without overnight ES (p=0.04) indicating ES improves sleep quality. The usability of the ES-shorts was good. In conclusion this study shows that overnight ES-induced muscle activation using ES-shorts in SCI is a new, feasible method that does not interfere with sleep. Overnight use of the ES-shorts might be considered as an important part of the daily routine in SCI.

Introduction

People with spinal cord injury (SCI) face several secondary physical problems such as pressure ulcers (PUs)[1]. PUs occur in up to approximately 80% of all people with SCI[2, 3]. PUs, in particular deep tissue injury at the buttocks, or more specific at the ischial tuberosities, increase the incidence of re- hospitalization and disability and cause a great decrease in quality of life [4]. As a result, approximately 25% of the total health care costs in individuals with SCI can be attributed to PUs[5]. Thus, it is of utmost importance to prevent PUs to maintain quality of life in persons with SCI and reduce costs. Continuous pressure under the buttocks, caused by inactivity and insufficient weight shifting when sitting, muscle atrophy, loss of sensation, ischemia and decreased subcutaneous oxygenation in the gluteal muscle are important factors contributing to reduced tissue viability and breakdown due to pressure and shear forces [6-12]. Measures to prevent PUs, such as wheelchair cushions and instructions to lift and shift weight frequently [13], are apparently insufficient as these wounds still occur. Electrical stimulation (ES) induced contractions of paralysed gluteal and hamstrings muscles have been found to decrease seating pressure, increase muscle mass [14,15] and enhance blood flow 1[6-19]. Therefore, ES seems to be a promising prophylactic aid in PU management.

Although studies on effects of ES have shown positive results, these studies have not translated into widespread clinical practice. It is interesting to study if ES can be made more easy to use in daily medical care. If ES could be made more practical to use, this might not only facilitate ES use in clinical practice, but also enable more high-quality studies to follow. A practical solution to the application problem how to use ES, was recently presented in a study by Smit et al.

(2012) showing the effects of ES on short-term interface pressure using electrical-stimulation shorts (ES-shorts®)[20,21]. In the shorts the electrodes are integrated, and automatically align over the skin, and in that way gluteal and hamstring muscles are activated non-invasively. Participants in the latter study indicated that they were rather satisfied with the ES-shorts and were willing to use the shorts in the future if positive effects were found.

The ES-shorts have not yet been tested for extended stimulation protocols, lasting longer than 3 hours, and only acute effects have been studied. Possible problem might be that muscles will stop contracting after prolonged ES-induced activation, due to loss of adequate contact between electrodes and skin or due to muscle fatigue. In addition the use of loose electrodes or ES shorts while sitting demands additional transfers which is undesirable as transfers generate high pressure on the gleno-humeral joint, possibly resulting in shoulder complains or injuries [23]. ES shorts are difficult to wear under clothes in a wheelchair. Therefore, the ES-shorts might possibly be better worn overnight instead of during the day in the wheelchair. In previous studies we have used other prototypes ES-shorts with a other (thinner) material used [20-22]. Daily ES in the wheelchair has several advantages over ES overnight and should not be 'dropped', but overnight ES could be used additionally. Overnight muscle activation does not demand additional transfers and does not at all interfere with daily activities. However, it is yet unclear whether prolonged muscle activation is possible, and whether overnight electrical stimulation has disadvantages, e.g. it may adversely affect sleep. In the present study we investigated whether overnight ES is a feasible method to activate gluteal, quadriceps and hamstrings muscles in a two-week experiment. The aims of this feasibility study in participants with an SCI were:

1. To evaluate whether ES still results in muscle contractions after 8 hours.
2. To study if overnight ES- induced leg muscle activation disturbs sleep.
3. To evaluate if the specially designed ES-shorts are user friendly and can be safely used in bed.

We hypothesized based on our previous studies and experience with the ES-shorts [20,21], that overnight ES-induced muscle activation, with use of the ES-shorts, is a user-friendly, feasible method that does not interfere with sleep, and that muscle activation is possible for an 8-hour period if sufficient rest in between the activation periods is allowed.

Methods

Participants

Eight individuals with SCI having a motor complete lesion (ASIA Impairment Scale A or B) and aged between 30 and 57 years participated in this study, approved by the local medical ethics committee. Characteristics of these individuals are shown in table 1 and 2. Gluteal and hamstring muscles skin under the buttocks, and spinal reflexes had to be intact, which was evaluated for all participants by one physician. Previous (plastic) surgery under the buttock area was no contra-indication for inclusion. Excluded were individuals with a flaccid paralysis and a-reflexia, a history of severe autonomic dysreflexia, current PUs under the ischial tuberosities, severe cognitive or communicative disorders, or intolerance for ES. The participants provided written informed consent.

Table 1: Participants group characteristics

	N or Mean ± SD (range)
Participants (M/F)	8 (7/1)
Age (years)	42.6 ± 9.4 (30-57)
Lesion level	C5- C8 (N=4) Th4- Th9 (N=4)
ASIA impairment classification	AIS A: 3 AIS B: 5
Time since injury (years)	14.0 ± 9.2 (2-32)
Body mass (kg)	80.2 ± 16.4 (61-115)

Table 2: Participant's individual characteristics

Participant	Sex	Age (years)	Body mass (Kg)	Lesion Level	AIS	Time since injury (years)	Stimulator current (mA)
PP01	M	40	83	C5	B	11	72
PP02	M	39	73	T4	B	20	60
PP03	M	37	70	C6	A	16	30
PP04	M	39	65	T6	A	18	48
PP05	M	38	61	T9	A	32	48
PP06	M	57	84	T7	B	4	60
PP07	M	30	91	C5	B	8	72
PP08	F	56	115	C7	B	2	72

Study design

A week before the intervention, participants were fitted with customized ES-shorts® (Axiobionics, Ann Arbor, MI, USA). They received instructions through demonstration and an instructions booklet on how to use and maintain the ES-shorts, and on how to determine if the muscles contracted as a reaction on the electrical stimulation. The individual stimulation protocol was determined. Participants followed a two-week, seven nights-a-week, ES protocol at home. The stimulation program automatically ended eight hours after starting, however, participants were allowed and able to stop the ES before the stimulation protocol was ended if necessary in case of any problem. Before the start of the 2 weeks of overnight ES, muscle contractions were measured by recording the changes in leg circumference. When a muscle contracts it will become shorter and thicker. Contractions are indicated by an increase in circumference. Directly after the ES intervention two questionnaires on sleep quality and one on usability were filled out. Four weeks after the ES intervention was ended these questionnaires were filled out again to measure sleep quality without overnight ES. See figure 1 for the time schedule of this study.

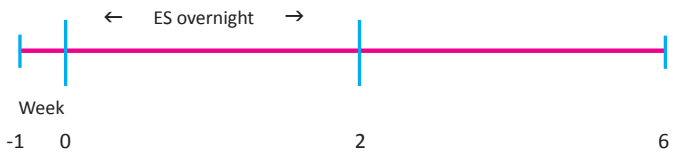

Figure 1.
Time line of 2 weeks of overnight ES-protocol. Before start intervention: fitting ES-shorts, set up stimulation protocol. Week: -1: Fitting ES-shorts and instruction. Measurement of muscle fatigue 0: start intervention of ES at home for 2 weeks. 2: Last day of intervention period: sleep quality, usability questionnaires. 6: Follow up 4 weeks after end of intervention. Questionnaire on sleep quality.

Electrical stimulation with the ES shorts

A portable electrical stimulator (Neuro Pro 8 channel, Axiobionics, Ann Arbor, MI, USA) connected with the custom-made ES Shorts was used to apply ES, delivered at standard constant voltage of 150 V. Using 35Hz bi-phasic impulse frequencies, a tetanic contraction of gluteal, quadriceps and hamstring muscles of both legs was induced with a square pulse form with one second slope up and one down. The current amplitude resulting in the best muscle activation was determined for each individual participant by increasing the amplitude in steps of 10mA to a maximum, without discomfort or excessive or painful muscle contractions. The electrical stimulator only activated if there was electrode-to-skin contact and contact between electrodes and stimulator. The stimulator's settings were kept constant during two weeks. The stimulator was connected to the ES-shorts with 1.5-meter long electrical wires, allowing the participant to place the stimulator next to his or her bed, for example on the bed table, while wearing the ES-shorts in bed.

The ES-shorts used in this study have been specially designed. They are made of partially elastical lycra material and have velcro flaps. When these flaps are untied the shorts can be fully folded open. The person putting the shorts on can simply lay down (e.g. as on a towel) and then connect the flaps to close the shorts around waist and legs. There are two laps around the waist and three around each leg. See figure 2 for the ES-garment (ES-Shorts + stimulator + wires). The shorts contain flat-embedded surface electrodes with (0.5 cm) small soft attachable pockets filled with hydrophilic granules (Soil Moist Granules®, JRM Cleveland Inc., Ohio USA).

Participants were instructed to moisture these pockets under a water tap for 10 seconds and then attach them to the marked places inside the open folded shorts. The moistured pockets then conducted well for at least 12 hours according to our own experience after testing this (on ourselves). The stimulators were programmed to deliver 8 hours of ES, with 1-hour stimulation cycles. Each cycle consisted of 30 minutes with 36 contractions, 10 seconds on and 40 seconds off (1:4 seconds duty cycle) according to Smit et al. [21, 22], followed by 30 minutes of rest, in an attempt to prevent major muscle fatigue, and allow muscles to keep contracting throughout the stimulation cycles. This cycle was repeated until 8 hours of stimulation and rest were completed.

Feasibility of the overnight muscle activation

Feasibility was tested in three ways: 1. Muscle contraction size and fatigue, 2. sleep quality and 3. the usability of the ES shorts with stimulator and wires when used in bed overnight.

Muscle contraction size and fatigue

Whether the ES-shorts were effective in inducing contractions for 8 hours was determined by questioning the participants what they noticed after 8 hours of muscle activation, and by

Figure 2.
The Electrical Stimulation garment (ES-Shorts). The arrows indicate the position of the electrodes. Left: front side with embedded electrodes and Neuro Pro Electrical stimulator. Right: Backside of the ES shorts. Below: The ES-shorts opened (inside view).

continuous measurement of muscle contraction sizes. For this purpose, a Futek load cell (LSB200, 25lb, JR S-beam load cell, Futek Inc., California, USA) was fixed around the participant's upper left leg, using a Velcro strap with elastic ends. The device was calibrated according to the manufacturer's instructions every time it was used. When leg muscles contract, the leg circumference increases as the muscle shortens and thickens, resulting in more strain on the load cell and subsequently a higher output (arbitrary units in Volt). The difference between the output during a contraction and during rest is indicative of changes in muscle cross section and muscular strength.

Occurrence of muscle fatigue was determined in two ways. Firstly relative contraction size was measured for each participant over the first two contraction cycles (of each 36 contractions; in total 2 hours).

Average contraction size over the first three and the last three contractions was calculated for both stimulation cycles. Fatigue was defined as a significant decrease of this muscle contraction size, by comparing both the last 3 contractions of one cycle to the first 3 ones of the next, after 30 minutes of rest. Recovery was calculated as the difference in relative contraction size at the end of cycle one and the average contraction size at the begin of the next cycle. Secondly all participants were asked if at the end of the night contractions of activated muscles were still visible.

Sleep quality

A Sleep Quality Visual Analogue Scale (SQ-VAS) (23) and the Pittsburgh Sleeping Questionnaire Index (PSQI)[24], both validated instruments, were administered at the end of the two-week intervention program and 4 weeks after ending the intervention, to evaluate whether overnight stimulation altered the quality of sleep. The SQ-VAS consists of 3 questions on sleep quality, the PSQI of 9 questions. The PSQI items are summed into a single number indicating sleep quality is either good or bad, with a cutoff point of 3. A lower score indicates good sleep, three or higher: bad sleep quality.

ES-shorts usability

All participants filled out a custom questionnaire containing 8 questions about overnight stimulation and the ES-shorts at the end of the intervention period (for questions see figure 6). Answers were given on a 5-point Likert scale ranging from 1 'I totally disagree' to 5 'I totally agree'.

Statistical analysis

Two repeated measures ANOVAs were used to determine differences in muscle contraction sizes between cycles. Firstly, the difference in average muscle contraction sizes of the first and the second cycle (2 within-subject levels) of the first night was determined. Secondly, the average of the final 3 contractions of the first cycle to the first 3 of the next cycle were compared (2 within-subjects levels). Average contraction size of the first three contractions (of the first cycle) was set as 100%.

To analyze the (SQ-VAS and PSQI-) questionnaires paired student-t-tests were used to examine differences between the answers directly after the intervention and after 4 weeks without overnight ES. The frequencies of answers on the questionnaire on the ES-shorts usability were described. All data are presented as mean ± standard deviation (SD), except the results of the PSQI. They were described as median with the range. Statistical significance was set a priori at a p-value ≤ 0.05. All data were analyzed using the statistical package IBM SPSS for IBM Mac software (SPSS Inc., version 20, Chicago, IL, USA).

Results

None of the participants developed skin problems due to the electrodes or the stimulation, or had complaints of autonomic dysreflexia during the overnight ES-induced muscle activation. None of the participants had problems or complains about unexpected muscle contractions (or spasms), nor problems with (handling) the wires. Some participants reported unexpected positive findings like decreasing of inflammation around Ischial tuberosities area, increased ability to sit throughout the day without pain, improved wound healing and improved bowel function.

Muscle contractions

In 3 participants, contractions could not be reliably measured. One participant had visible contractions but extreme atrophied legs, with hardly any muscle volume left. Two participants had spasms due to the induced muscle activation, causing their contraction data to be unreliable. In 5 participants mean contraction size in the first cycle revealed to be significantly larger, compared to the second cycle (p=0.03), with average relative contractions being 76.7% (±14.1) in the first cycle, and 66.9% (±27.2) in the second. Contractions at the begin of the second cycle were 79,5% (±18.7) and significantly larger compared to contractions at the end of the first cycle, 63,7% (±21.7) (p=0.00), indicating muscle fatigue occurred due to ES-induced activation but recovered after 30 minutes of rest. Finally, contractions were detected at the end of cycle one and two 63.7 (±21.72) and 57.3% (± 23.7) respectively, and muscle contractions could still be detected at the end of 8 hours of muscle activation according to all participants. In figure 3, a typical example of two contraction cycles of one participant is shown.

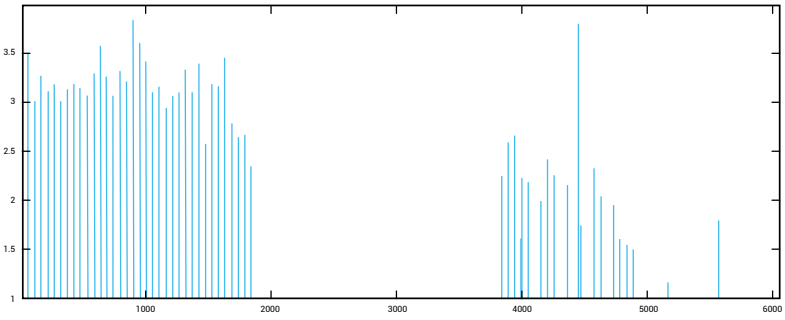

Figure 3.
Example of muscle contraction measurements of 2 cycles of one individual Two times 30 mins of contractions with 30 mins of rest in between. X-axis: samples (over time); Y-axis: Relative contraction size.

Sleep quality

Result of the PSQI questionnaire revealed that poor sleep quality was reported by 3 participants directly after the intervention, all being within only two points from the good sleep quality threshold, and poor sleep quality was reported by 4 participants in follow up, with scores between 3-5 points from the threshold. For the group, overall sleep quality of participants was poor, median 4 (2-7) during intervention and poor: 5 (1-10) during the month without the intervention.

Results of SQ-VAS are presented in figure 4. Sleep quality after 2 weeks of ES was 11.6% (significantly) better compared to 4 weeks follow up without ES (week 6): 66 to 75 [0-100] (p=0.04). Scores for tired versus fit did not (significantly) differ between week 2 or 6, indicating (feelings of) fitness did not alter due to ES induced muscle activation. Score for ES disturbance of the night's sleep was 82 (0-100), in favor of not disturbing the night's sleep.

ES-shorts usability

Results of the usability questionnaire are presented in figure 5. The colored bars behind the separate questions indicate the number of answers of the 5 categories (from 'totally agree' to 'neutral', to 'totally disagree'). Seven of 8 Participants (87.5%) needed help to put the ES shorts on. Seven (of 8) Participants (87.5%) reported that ES is totally not painful. All (100%) stated ES did not prevent them from falling asleep. Seven participants (87.5%) found stimulation and contraction of the muscles pleasant, 1 responded neutral. Seven participants (87.5%) as well indicated they were willing to use the ES shorts in the future if effects are proven positive, 1 responded neutral.

Discussion

This study showed the feasibility of overnight ES in people with an SCI. Applying ES overnight using specially designed ES-shorts is possible and safe. None of the participants stopped with the intervention during the 2 weeks due to any kind of problem. No pain, skin problems, no disturbing involuntary movements of the legs or trunk, and no symptomatic autonomic dysreflexia occurred in any of the 8 participants during the 2 weeks of ES.

Using the ES-shorts, muscle contractions decreased during the stimulation cycles, which is most likely due to fatigue of fast fatigue type 2 muscle fibers. After SCI, composition of muscle fibers in muscles below the lesion level shifts towards fast fatigue muscle fibers [33, 35, 51]. As a result, contraction size is likely to decrease over time after repetitive contractions. Although contractions decreased during stimulation, contractions were still detected at the end of stimulation cycles, indicating that (type 1 and type 2a) muscle fibers were active throughout the stimulation period. In addition, muscles recovered in between stimulation cycles, as contraction size after 30 minutes of rest, at the beginning of the second cycle were significantly larger than at the end of first cycle.

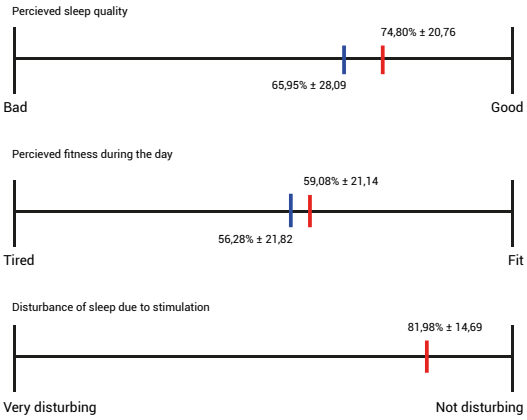

Figure 4.
Sleep Quality Visual Analogue Scale score. Week (wk) 2 (red): after 2 weeks ES. wk 6 (blue): follow up 4 weeks after ending ES. There is a significant difference for perceived SQ with ES (75%) compared to without (66%).

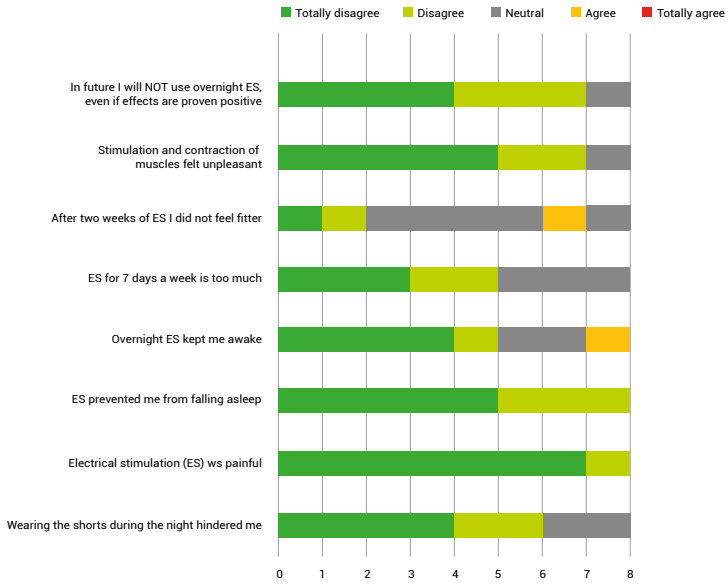

Figure 5.
Questionnaire on ES shorts usability.

This study also showed that overnight ES induced muscle activation, in people with SCI does not disturb sleep. Average sleep quality was even somewhat better during ES compared to sleeping without ES.

Most (7 of 8) participants even indicated they would like to continue overnight use of the ES-shorts in the future, as they (also) experienced improved sleep quality. Known is that people without SCI are physically active during the night while asleep [49], and moreover use more muscles while being active during the day than people with an SCI do or can. Possibly the improvements seen in sleep duration and quality in our participants are related to the increased muscle activity, the related physiological changes and to the catabolic process caused by the muscle activation. It might be as result of the physiological muscle breakdown that occurs during physical activity. The body requires a deeper and more restful sleep to repair the damage. Gebhart et al. [49] showed that in 114 abled-bodied participants physical exercise contributes to better sleep quality. A six-week moderate physical exercise, program, conducted weekly, significantly improved sleep quality, daytime mood, depressive symptoms and vitality. Derived from PSQI sub scores, the intervention group reported increased sleep duration, shortened sleep latency, fewer awakenings after sleep onset, and overall better sleep efficiency compared to controls.

The attained scores were well sustained and enhanced over a time that lasted through to the follow-up 18 weeks later. These findings in abled bodied to our opinion also have implications concerning healthy lifestyle approaches for people with an SCI. In summary related to present study; ES-induced muscles contractions, as a form of physical exercise, may cause deeper sleep.

The usability of the ES garment was good, and even some unexpected positive findings were reported. Most participants were enthusiastic about using the ES-shorts, and the wires did not hinder them in bed. All participants had placed the stimulator connected to the ES-shorts on the bed table next to their bed. The ES-shorts were specially developed, with the alignment of the electrodes directly over the skin. The current prototype is difficult to wear under pants, but developed and suitable for use in bed. Although they are, with adjustable Velcro flaps, relatively easy to put on, 7 of 8 participants needed help to do this. This was caused by limited hand function or trunk stability problems, in combination with (initially) being inexperienced in handling the shorts. In our study the size of the used shorts was not perfect for everyone. In some participants, the circumference of the upper leg was too large, causing the shorts to fit sufficiently, but not perfectly. This did not have a negative influence on the effectiveness of the muscle activation, but made wearing the shorts a little less comfortable. One participant recommended the use of a thinner material than the Lycra material used, to make wearing the shorts possibly more comfortable. In future use individually fitted ES shorts should be made to avoid fitting problems.

Clinical implications of this study concern the challenge to lower the incidence of PUs in SCI due to sitting. As mentioned in the introduction: ES induced contractions of paralysed gluteal and hamstrings muscles have been found to decrease seating pressure, while sitting in the wheelchair due to contraction induced changes in muscle shape and tone. Moreover, repeated

muscle contractions also increase muscle mass [14, 15] and enhance circulation [16-19]. Therefore, ES seems to be a promising prophylactic aid in PU management. We believe that the nightly use of the ES-shorts can be an important part of the daily routine of people with SCI, in addition to the normal measures already taken to prevent PUs. The ES-shorts do not reduce IT pressure when used lying (in bed, overnight) but do generate the positive physiological effects of muscle activation and training, like mentioned above. Especially the prolonged period of 8 hours of muscle activation is effective in increasing tissue oxygenation and reduction of muscle atrophy of the activated muscles of the buttocks [16,20,21]. The sample size in this study was relatively small but large enough for this pilot study on feasibility. Participants in present study were enthusiastic and experienced using the shorts overnight as not at all troublesome. All but one intended to continue using the shorts after finishing their participation in this study.

No training effects of the intervention program on fatigue were found. Some participants in present study stated that muscles were 'easier to activate' throughout the night as the intervention progressed. We haven't objectified these (subjective) findings. It is interesting to enlarge the period of applying ES [16, 27]. A 2-week period of muscle activation is probably too short to find significant physiological training effects of activated muscles: larger, stronger, and with improved circulation. For example Chilibeck et al. [16] showed that in 6 participants FES-Leg cycling exercise 30 min, 3 times a day for 8 weeks caused a significant fiber area increase of 23% as well as a significant capillary number increase of 39%. Mawson et al. 50 in 29 participants showed that ES (High Voltage Pulsed Galvanic Stimulation) gave a significant dose-related increase of the perfusion pressure gradient in the capillary beds of the activated muscles. Within 6 weeks up to 35%.

Future studies should focus on prolonged ES overnight using the effective ES-shorts and protocol, used in this study. Regarding the studies on physiological training effects we suggest a minimal period of 6 weeks [38,41,43,45,46,50]. We performed a power analysis (ANOVA two tailed, r=0.8; significance level 0.05) that showed that two groups of each 8 participants could reveal a clinical relevant 10% increase in muscle mass, blood flow and muscle oxygenation. Although this is a difficult challenge more studies (randomized clinical trials) should follow to determine the clinical relevant increase needed to decrease the incidence of PUs.

Conclusion

Overnight electrical stimulation of leg muscles is a safe and feasible method of inducing paralysed leg muscle contractions in people with an SCI. No side effects or problems occurred during a 2-week overnight stimulation protocol. The muscles were successfully activated for 8 hours. Muscle fatigue occurred due to ES-induced activation but recovered after 30 minutes of rest. ES did not disturb, but even tended to improve sleep quality. The usability of the ES-shorts, specially developed for this study, was good. In the continuing challenge to lower the incidence of PUs in SCI due to sitting, future studies should focus on prolonged ES overnight in order to study a possible increase in muscle volume, blood flow and muscle oxygenation, and subsequent decrease in the incidence of PUs.

Authors statements

The authors declare no conflict of interest.
There have been no competing Interests, and no external or comercial sources of funding.

This study involves human subjects, and was ethically approved on 23rd of May 2013,
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General discussion

Christof AJ Smit

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An anecdotal case report

This is the story of one of my patients, 38 years old when writing this. In 2002, when he was 25 years old he was diagnosed with a traumatic paraplegia Th 11 (American Spinal Cord Injury Association Impairment Scale, or: ASIA Impairment Scale] AIS: A) due to a car accident. After 3 months of inpatient rehabilitation he lived wheelchair bound and self-supporting. At present he works as an assistant lawyer at an office, and is able to drive a car. He got married and has two children. In 2007, five years after his SCI, he developed his first ischial tuberosity pressure ulcer. He had plastic surgery and was re-admitted to the rehabilitation center. To enable wound healing, an absolute relief of pressure was indicated to ensure good wound healing. Therefore, he was not allowed to sit at all. He described those weeks in the rehabilitation center lying on his belly, moving around a bit on a 'rolling stretcher (brancard)' as 'terrible', despite good care and nice people around him for his support. He was unable to move freely (in his own wheelchair), mentally getting depressed, experiencing difficulties to keep up the contacts with family, friends, and colleagues at work. About 8 weeks after surgery, his wound was healed and he was able to start to sit in his wheelchair. Multidisciplinary effort was done to prevent occurrence of a new wound. His sitting position in his wheelchair was analysed, a new cushion to sit on was advised and delivered. Again instructions were given to regularly perform pressure-relief movements, such as bending forward.

Twelve weeks after admittance to the rehabilitation center he was discharged and went home again. In the following two years, he visited our outpatient clinic several times for regular check-ups. When I saw him about three years later, he presented himself with a pressure ulcer at the same ischial tuberosity again. The entire procedure started again, with a dramatic impact on daily family life, his working life, and most of all, his self-efficacy. This led imaginably to distress and despair. At that time he literally said: 'my life has been ruined'.

Recently he visited my out-patients ward, and told me he had been activating his leg muscles in order to prevent PUs, using electrical stimulation a few times per week on both legs. It pleased me to see him in this good state: happy, in good health and fit. He has had no new PUs for 7 years now.

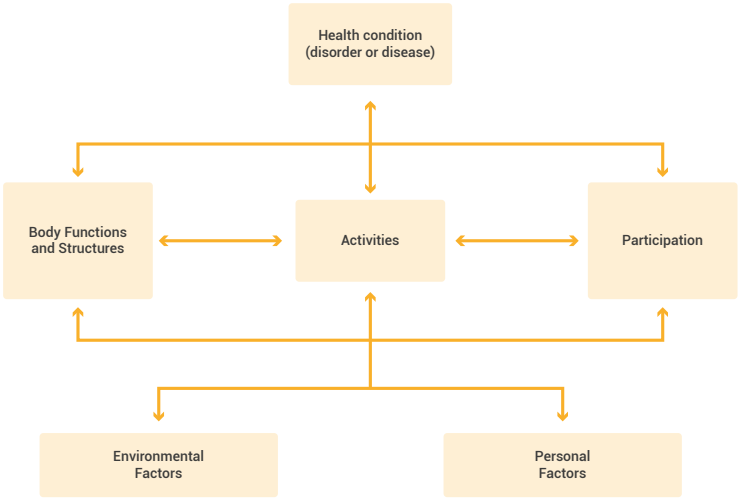


Figure 1: International model for the classification of functioning and health (ICF mode)

Pressure ulcers have a tremendous negative impact on functioning

Rehabilitation consultants, nurses and paramedics working in the field of SCI rehabilitation will undoubtedly recognise the problems indicated in the above anecdotal case, and more in general the problem of pressure ulcers (PUs) in people with an SCI. It is the most prevalent complication in SCI. In the literature, numbers on the incidence differ, from 62 to 85% of the individuals with SCI developing a PU during lifetime, mostly at the sacral or ischial tuberosities (IT-) region[1,2]. According to the Model SCI System Sta istical Center, approximately 15% of individuals with SCI will develop a PU within the first year of injury and approximately 27% over the first 25-year period post injury[1]. Even up to 85% of adults with SCI will develop a PU at some point during their lifetime[3-6]. Additionally, 40-80% of those who develop a PU will have at least one recurrence[2,4].. All individuals with SCI, certainly those with complete lesions, but also those with incomplete lesions are considered to be at high risk of PU development throughout their lifetime[2,4,5].

Where my patient in the anecdotal case report said ‘his life was ruined’, in general the occurrence and treatment of a PU, especially on the IT’s, with mandatory bed rest to allow wound healing, has a tremendous negative impact on the individuals’ functioning. In the figures

1 and 2 all domains of the international classification of functioning (ICF)-model are shown, in which can be seen that a PU interferes with all the domains, and negatively influences body functions and structures, activities (of daily living), and participation (like occupational duties). Furthermore PUs generate high health care costs for the community[1,2,4,5]. In severe cases, PUs may even be life threatening[2].

The hypothesis prior to this thesis was that ES-induced muscle activation of the buttocks and leg muscles would be a useful method to reduce risk factors to eventually prevent development of PUs of the soft tissue covering the IT's. This generated several practical and research questions about this method. Answers to these research questions are incorporated in themes in this general discussion. The most important findings of the studies performed will be united and discussed on their implications and clinical relevance. Also limitation of the studies are elucidated and discussed, and furthermore recommendations for future research are provided.

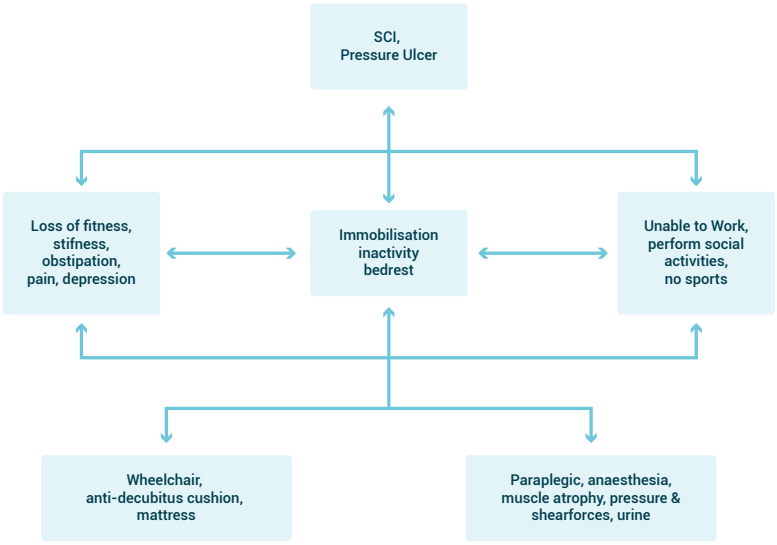


Figure 2: ICF model for the man with an SCI and PU in the anecdotical case report

Conceptual PU prevention model using electrical stimulation (ES)

As written in the general introduction, a conceptual model was created based on the literature, and shows that pressure causes a PU to occur, when tissue tolerance for deformity is exceeded. The study results in this thesis have added to the strength of this model. In chapter 2 an overview of literature is presented, based on this model. Results will be discussed below.

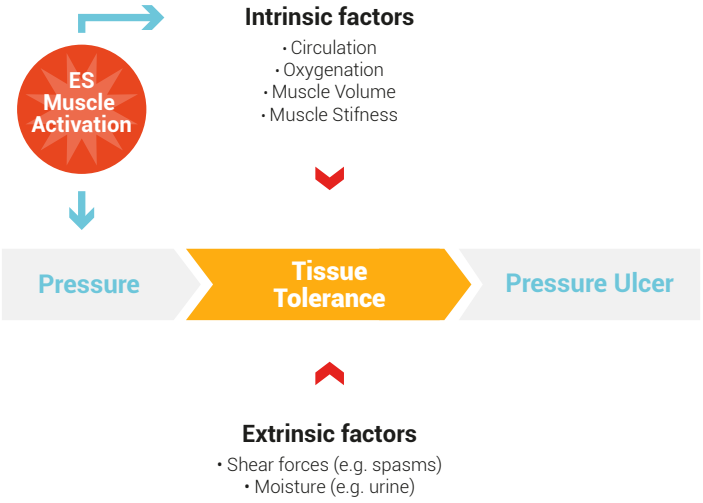


Figure 3: Conceptual model of the etiology of a PU and the effects of ES-induced muscle activation

Effects of ES- induced muscle activation

We have studied the acute effects of ES-induced muscle activation in order to develop a new method. We have delivered transcutaneous electrical impulses, activating local nerves to generate a spinal reflex, inducing muscle contraction.

The studies in this thesis have shown that due to (repeated) muscle activation high ischial tuberosities (IT)-pressure decreases, skin and muscle peak blood flow increases, as well as oxygenation.

Decrease of ischial tuberosity pressure

In chapters 3-5 ES-induced activation of gluteal or gluteal and hamstrings muscles caused a decrease of IT-pressure, together with an increase of pressure in the area of the upper legs. Of course the total amount of surface pressure remained the same as ES does neither change the persons weight, nor the gravity. The pressure was relocated from the ITs to the front of the sitting surface. This desirable relocation did not cause any skin problems in this area in the 24 participants (total of participants in one or more of the studies in the chapters three to seven), as there are no bony prominences at the hamstring site near the knees. This relocation is caused by two mechanisms. First the change in shape, tone and form of these muscles while activated compared to relaxed, secondly the extension movement in the hip due to acute gluteal and hamstrings muscles contraction.

During multidisciplinary SCI rehabilitation PU preventive measures are taken. As written in the general introduction, for example, education on the development and the prevention of PUs is given, and persons with an SCI are taught how to perform adequate transfers (for example from bed to wheelchair and back), and to avoid skin or tissue damage due to shear forces. Furthermore, these individuals learn to perform pressure-relief movements (PRMs) while sitting in the wheelchair, such as bending forward, to release pressure of the ITs, and restore compromised tissue and blood flow. In chapter 6 (page 96 and further) is shown that ES-induced muscle activation in people in a wheelchair seems not always as effective in reducing peak interface (sitting) pressure, as pressure relief movements (PRM's) (like bending forward) are. PRMs though have some disadvantages: performing them is not always socially accepted or possible, and even impossible, for example when driving a car. In addition, performing a PRM by lifting the whole body will increase the risk of shoulder injury[15,16,17] ES has several advantages. The frequency of this muscle activation is so much higher than the frequency in which on average a person with an SCI performs a PRM (Reenalda 2009, 2010)[13,14], that in the longer term ES induced muscle activation is much more likely to be effective in preventing PUs of the buttocks than PRMs are. Moreover, muscle activation has several other positive effects, like increase of muscle volume and increase of blood circulation. Furthermore it is likely that effects (of IT pressure relief due to muscle activation) will even increase when muscles are better trained[19, 20].

The etiology of PUs is complex. Several factors contribute to the tissue tolerance (figure 2). We do not know what amount of IT-pressure reduction is clinically relevant in reducing the incidence of PUs. This ultimate goal remains a challenge for future research. See 'future perspectives' further in this chapter.

Improvement of muscle quality, circulation and oxygenation

Muscles in good condition are better perfused and oxygenated, and likely continue to contract after prolonged activation. Better circulation and oxygenation conversely lead to better muscle condition. As in normal ('non-paralysed') muscle activation, there is sufficient evidence for beneficial training effects when ES-induced exercise is performed chronically. 'Normal'

Physiological training effects of ES-induced muscle activation have been found on fatigue, type of fibers, and/ or tissue quality (volume, perfusion, stiffness)[21,23, 24]. When a muscle is more activated the muscle will get healthier, better perfused, stiffer etc. Important finding is that every mentioned effect will only occur in activated muscles and only endure when activation is sustained lifelong[24-26]. These are physiological effects that occur only in the trained muscle and last as long as the muscle is being activated.

Participants in the study in chapter 7 (page 110 and further) reported that after 2 weeks, (leg-) muscles were easier to activate than at the start of the intervention. This might be a training effect that is also found in in other studies, but might also be the result of an improvement of nerve conduction according to Lee et al (2015)[27], or reduction of fat mass[28]. The use of electrical stimulation to produce force from a muscle results in more rapid fatigue, that is, loss in the force-generating ability of the muscle due to prior activation, than comparable voluntary contractions[23]. In addition, after SCI, paralysed muscles often become more easily fatigued[18,19,29]. Consequently, rapid fatigue has been one of the factors limiting the clinical effectiveness of ES in paralysed muscles as in SCI.[19,21,22,33]. However, after prolonged training (read: ES-induced muscle activation) muscles are less easily fatigued and contract stronger and longer[21,22,25,33] .

It is also likely that ES-induced training of these muscles over time will have a positive effect on fatigue, and training schedules can be adjusted into more intensive ones after some time. Chou et al (2007)[29] and Dreibati et al[25] (2010) found that long-term effects of ES to muscles are a conversion of fast-twitch type 2 muscle fibers, predominant in atrophied muscles, into slow-twitch type 1 muscle fibers. ES-induced exercise training has been shown to markedly increase resting blood flow in the femoral artery of individuals with SCI[26,32,33].

Loerakker et al (2013)[32] described the correlation between stiffness and the increased risk of tissue to break down due to deformation by pressure and or shear forces. Brief summary: the stiffer the tissue, the lower the risk of a PU to occur. It is known from physiological principles that training induces muscle hypertrophy and a fibrogen decrease in muscles, making the muscles stiffer with more muscle mass. Therefore, indirectly ES-induced muscle activation likely causes a decrease in the risk to develop a PU[32]. No study, as far as known, has yet been performed that investigated the relation of ES induced muscle activity and muscle stiffness.

Taylor et al.[31] showed that thigh blood flow, which was circa 65% of normal levels before the training period, returned to normal levels in a group of patients with SCI who participated in a training program. In addition, a study by Hopman et al.[42] revealed that the increased leg vascular resistance found in patients with SCI was reversible towards normal values by training the paralysed legs three times per week using ES of the muscle during a 6 week program. Skin and muscle blood flow appear chronically augmented after prolonged ES-induced exercise training, but it is important to realise that only activated muscles show an augmented blood flow[26], indicating that, as mentioned above, it is essential to activate those areas that are at risk of PUs, and continue doing that life long[24-26].

Electrical stimulation protocol

Which muscles should be activated for the best result?

The results from chapters 2 (page 22 and further) and 4 (page 70 and further) indicate that ES-induced activation of only gluteal muscles generates less pressure redistribution than the activation of both gluteal and hamstrings combined. This is likely caused by two mechanisms: first mechanism is that of the changes in tone and shape of the activated muscles. There will be a larger effect when more muscles are (adequately) activated. Second mechanism is that the extension in the hip with lifting effect on the buttocks, when activating the hamstrings in a sitting position, results in a lift of the body of the seat. The study in chapter 5 aimed to answer two questions: to compare two protocols, and to describe the acute effects of muscle activation compared to rest on sitting pressure. Results showed that ES-induced muscle activation caused pressure decrease and that of these two protocols the one with more rest in between stimulation gave better results.

In the feasibility study of overnight muscle activation in bed (chapter 7), we activated gluteal, hamstring and quadriceps, in both legs, causing desirable co-contractions of both hip and knee extensors. We applied ES to the participants while they were lying in bed, activated the leg muscles using six electrodes for each leg. This resulted in a maximum number of muscles to be activated with the 8-channel stimulator we used, in combination with minimal movement of the legs due to isometric co-contractions. There was no need to restrain the (lower) legs in bed. Fortunately, the results showed that sleep quality was good during the nights with ES, and participants encountered no problems. In literature we have found no other study applying overnight ES in lying position while sleeping[34,35].

Ferguson et al[17] (1992) activated the quadriceps muscles in the wheelchair, applying ES to the quadriceps with the lower legs restrained, causing knee and hip extension, elevation of the buttocks and decrease of interface pressure. In our studies we choose not to restrain lower legs and/ or the feet as we not only considered fixing the lower legs to the footrest undesirable and unpractical, but also potentially hazardous since it might increase the risk of causing PUs to occur due to the effects of restraining and immobilizing the legs. We found no other studies describing the activation of leg muscle groups while sitting, other than gluteal and/ or hamstring muscles.

Concluding we cannot state which muscle can be activated for the best pressure redistribution. Our results showed that in a wheelchair ES-induced gluteal and hamstring muscle activation caused more pressure decrease than activation of the gluteal muscles only. While lying in bed we cannot conclude which muscles can be activated for the best result, as we did not compare results of activation of separate muscle groups. We did find, however, that similar cocontraction of a- and antagonist leg muscles, i.e activation of both extensors and flexors at the same time gave muscle activation without disturbing leg movements or disturbing of sleep.

Stimulation parameters

The efficiency and efficacy of ES depends on its protocols and parameters, such as the nature of the application technique, the stimulation frequency, intensity, duration, rest intervals, as well as the number of times the muscle is simulated in a day or a week. The combination of this great number of parameters, in combination with the variety of differences among the participants in (our and other) study population(s) undoubtedly resulted in sub optimal individual protocol settings. It seems impossible to determine the absolute optimal settings as there are too many parameters. Nevertheless, knowledge of (general) physiological training effects of (healthy) muscles[29,30,31], in combination with results from previous studies in this field, helped us to determine a protocol that worked well. Despite inevitable suboptimal settings we were able to show positive effects in all the studies we have performed, indicating our protocols (Chapters 3, 4, and 5) were at least adequate.

Ratio activation and rest ('on-off ratio')

We compared two ES protocols in chapter 5 (page 82 and further) of this thesis, and based on the protocol used by Bogie et al[12], we activated the muscles with an on-off duty cycle of ES of 1:1 s in a 3-min period, with a 17-min inter stimulation intervall[5,25]. This is also approximating the frequency of weight shifting Reenalda et al (2010)[7,8] recommended for wheelchair users at risk of tissue breakdow. We determined fixed (equal) parameters for the two protocols, and only varied rest time between them. Fixed parameters were: 150 V potential, adaptable to the resistance of the skin and tissue, in order to keep a fixed current amplitude, 50 Hz frequency, biphasically with a square pulse form with one second slope up and one down. One protocol had a stimulation-rest interval of 10 seconds 'on', 10 seconds 'off' (ratio: 1:1), during the 3 minutes of ES and the other 10 seconds 'on', and 40 seconds 'off' (1:4). Results showed that protocol 1:4 had preferable effects over protocol 1:1. We showed that over 3 hours of stimulation in this protocol (1:4) participants' gluteal and hamstring muscles kept contracting without marked muscle fatigue. This suggests that probably perfusion, as well as oxygenation, was sufficient for this 1:4 protocol, during the 3 hours of testing. These results confirmed those in studies of Gerrits et al[22,33], and Janssen et al[26], also showing the improvement of blood flow and oxygenation in stimulated paralysed muscles of people with SCI. This 1:4 duty cycle has not been compared with other protocols and although this ratio 'worked well' and proved to be adequate in our study, and better than the '1:1 protocol', we do not know if this is the optimal stimulation-rest ratio.

Central question to be answered is how much recovery time muscles need for continued activation. A perfect combination of frequency and duration of the electrical impulse delivered to the muscles will give the optimal activation intensity combined with rest, and optimal balance between effects and side effects. More and stronger muscle contractions will give more effects, but too much muscle activation will lead to pain, undesirable movements, and early muscle fatigue[18]. Once the maximal current output intensity of the stimulation is reached, muscle performance will markedly decrease and become insufficient to maintain exercise[21].

Maybe another duty cycle, like for example on–off ratio 1:6, and or rest period shorter than 17 min will have even more preferable effects on pressure relief versus fatigue. Training effects will likely change this ratio as well, enabling more frequent activation with less fatigue and more effects. This needs further investigation.
We found studies describing 'classical' 20-minute training sessions with many contractions (60 or more per minute) used in fitness programs[20,25,33]. This does not seem appropriate for training in (clinical) rehabilitation programs for paralysed muscles, as these sessions are too intensive for the untrained paralysed muscles, and therefore ineffective, as muscles will stop contracting when they are overstimulated and fatigued[18,33,36,37].

Stimulation pattern
Janssen et al. in 2004 compared four different stimulation patterns to activate paralysed muscles[26]. (1) Standard pattern with ramp modulation, (2) a pattern with no ramp modulation, (3) a pattern with no ramp modulation but with an initial doublet, and (4) a pattern with a middle doublet. During the first three minutes of ES-induced leg muscle activation to induce cycling movements of the legs (leg cycling exercise; LCE), the current amplitude was significantly higher with the standard stimulation, suggesting that stimulation with no ramp modulation produces more force at the same submaximal current amplitude. But none of these stimulation protocols resulted in significantly improved cycling performance compared with the standard pattern, with ramp modulation, which is the same we used in our studies (chapters 3-6).
Taken together there is no undisputable recommendation on what stimulation protocol gives optimal results. State of the art knowledge is based on the combination of 1) basic physiological training principles, 2) gained knowledge in other studies, and 3) results in our studies, that weekly training for 3 times per week with a minimum of 30 minutes per training session is adequate in improving circulation and oxygenation, and counteracting muscle atrophy. The used 1:4 seconds on-off protocol (in the chapters 4 & 5) proved to be adequate.

Electrical stimulator
We have used a Neuropro eight-channel electrical stimulator (Neuropro, Berkelbike St. Michielsgestel, The Netherlands) connected to the ES-shorts. As mentioned previously, stimulation was delivered biphasically at 50Hz to induce a tetanic contraction. The stimulator was relatively small and easily portable, and has the ability to activate eight muscles at once, but it is too large to be put for example in one's pants pocket. Furthermore, it hindered some participants in more than one study, as it is difficult to operate the device as it does not work 'intuitively'.
This device is suitable for use in scientific studies, but not for use in daily life by end users. Future challenge therefore is to technically improve this electrical stimulator. This can be done by reducing the size of the stimulator and its weight, but most important by improving its user-friendliness, for example by developing a touch screen. There are several commercially

available electrical stimulators available already (e.g.: Compex®, Wasomed [Reha Move]®, Bioness®) that are more user friendly than the one we used in our research, shown in the picture below.

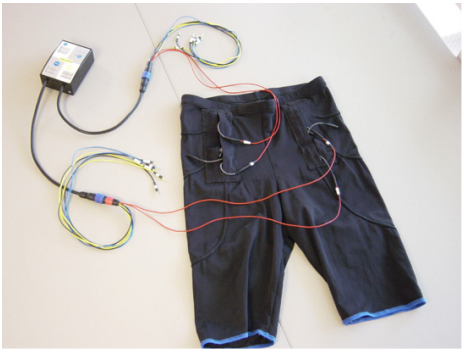
Neuropro 8-channel electrical stimulator. Suitable for research purposes, but not less user friendly for daily (clinical) use.

ES-garment

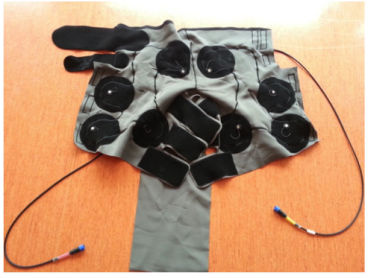
We used specially developed ES-garment or 'ES-shorts' with built-in electrodes connected to a portable stimulator. They have only been used in our studies, but hardly in clinical practice. A Canadian research group (Mushahwar et al.) that has developed the 'smart-e-pants', which are similar shorts. There are several reasons to be enthusiastic about the ES-shorts. This method is non-invasive, the costs are relatively low and electrodes are fabricated within the ES-shorts, and therefore do not have to be placed repeatedly. The ES-shorts were found to be feasible for the application of ES in daily life situations. This new method has a major advantage over systems such as the dynamic seating systems[7,8], in the sense that it can be used independently from the daily use wheelchair. The ES system 'travels' with the person without the need to make any changes or arrangements. It can be used while sitting on the couch, while sitting on the plane during a 10-hr flight, while sitting in a sports wheelchair, etc. In addition to that advantage, no lifting is needed, which reduces the load on the shoulders and with this the risk of shoulder and arm injuries9. Moreover, the ES shorts can be worn under the regular clothes. Participants in every study of this thesis (n=32) all, without exception, stated they would wear the ES-shorts with the stimulator in daily life, even all day long, if it helped them to prevent PUs. Feedback from participants enabled us and the manufacturer of the ES-shorts in Ann Arbor, Michigan, USA, helped us to carry out improvements and to develop the ES-shorts. In total we have used three proto types, shown in the figures below. Main improvements were made in respect to the use of ultrasound gel, and to the ES-shorts themselves. Inserted into the appropriate small pockets had to be about 2 millilitres of the ultrasound gel, which has been replaced by using previously moistured hydrophilic granules instead. The gel caused 'wet' spots in some participants' clothes, which of course is undesirable. The granules also conducted electrical pulses well, and are as easy to be put in the pockets as the gel is. After moistening under the water tap for 10 seconds these granules conducted well for at least 8 hours, as was shown in the study we performed on the feasibility of prolonged overnight muscle activation (chapter 7). The ES-shorts were adapted with an open flap at the front, which enabled both intermittent (self-) catheterisation of the bladder, or the better positioning of an indwelling bladder catheter. At the same time the open flaps made the ES-shorts easier to put on.

The ES-shorts used in chapter 7 were specially made for use in bed with no clothes on. They are made of slightly thicker material than the 2 other types of ES-shorts (in chapters 4,5 and 6). They can be completely folded open, like a towel, and put on using Velcro flaps. At the moment the usability of the ES shorts seems appropriate and they can be used in daily life. In the future feedback from users will undoubtedly help to optimise the ES-shorts even more. None of the participants reported side effects wearing the ES-shorts while receiving ES, but some participants reported practical problems, such as applying the ultrasound gel or handling the stimulator. In a controlled setting like in a hospital or rehabilitation clinic conventional stimulators with loose electrodes could also be used to apply ES, in stead of using the ES shorts, although we believe even in a professional and controlled setting like that, the ES-shorts provide more advantages compared to the use of loose electrodes.

Prototypes, examples of two ES shorts used. This prototype can be used under clothes, but also be worn as 'normal shorts'. Used in chapter four and five.report



ES-shorts for overnight use. Not developed to wear under clothes. Used in chapter 7



Positive side effects of ES induced muscle activation

We have experienced no negative side effects or problems during the studies we performed. Fortunately, no skin problems or (symptomatic) signs of autonomic dysreflexia have occurred. This of course is good news. In other studies (literature review chapter two) in total, (only) four out of the selected 34 (preventive) studies reported on (potential) adverse events of ES. Among these four studies, two studies delivered ES using surface electrodes[29,30], while one study used a neuromuscular ES implant12 and one used a sacral anterior root stimulation implant (SARS)[13]. All four of these studies reported no adverse events experienced by the participants in their study. The (potential) adverse effects described were skin problems using electrodes attached to the skin or technical problems with the implanted system.

Participants, in contrast, did report positive side effects. Not just a few, but without exception all participants of the separate studies (n=28). Some of the frequently heard citations of these beneficial side effects from ES-induced muscle activation were: 'I feel less tired', 'I have more energetic feelings, 'ES improved my fitness and well-being, even hours after finishing ES induced muscle activation'. These rather remarkable findings could be the result of several mechanisms. They will be discussed here in a random order.

1. ES-induced increase of the (relatively low) blood pressure.

Compared to the able-bodied population mean arterial blood pressure is lower in people with an SCI, especially in those with a tetraplegia[38,39,40]. This is due to several effects following the loss of sympathetic control of the vascular system and the control of the renin-angiotensin system. Angiotensin II and III exert their action on blood vessel walls, increasing muscle tone and, in turn, cardiac contractility of the heart. Consequences of a chronic low blood pressure are tiredness, dizziness, weakness and even fainting[38,39,40]. Exercise bouts performed voluntarily have been shown to increase blood flow to the active muscles at the onset of exercise, adapting to a steady value appropriate for the metabolic demand[41,42]. We measured blood pressure (BP) in the study (chapter 6) where we compared pressure- relief movements (PRM's) with ES, after the PRM's had been completed, just prior to starting the 3 min of ES, and when ES was being applied (2 minutes after starting the stimulation protocol). Every BP measurement was done twice and results were averaged into one value for systolic, and one for diastolic BP per participant in rest and with ES. Unpublished data in table 1 show that ES-induced muscle activation significantly increased systolic BP ($p=0.03$), and not significantly changed diastolic BP, although there is a tendency to increase. Mean blood pressure increased during ES induced muscle activation.

This can possibly be a 'silent autonomic dysreflexia'. None of the participants with an SCI at level Thoracic 6 or higher in our studies (chapters 3-7) had complaints (headache, malaise) or symptoms (red skin above the SCI, pale below, swetting) matching the (potentially dangerous) complication of autonomic dysreflexia. We believe more research needs to be done to investigate this.

Table 1: Blood pressure differences between rest or with electrical stimulation (ES). A significant in- crease of systolic blood pressure due to ES induced muscle activation is shown. An asterics (*) indicates a significant correlation: $p<0.05$. SD = standard deviation.

	Mean blood pressure (mmHg)	SD	N	Significance increase
Diastolic rest	66.5	11.3	8	0.084
Diastolic ES	70.5	11.4	8	
Systolic rest	104.6	24.7	8	0.034*
Systolic ES	115.2	15.6	8	

2. Decrease of venous pooling.

Several studies have shown that ES-induced muscle activation improves blood circulation and prevents venous pooling, leading to reduction of orthostatic hypotension, which has a correlation with tiredness and fatigue[43-46]. Originally developed as an alternative deep vein thrombosis prophylactic technique, Glaser, et al.[8] (1991) demonstrated that rhythmic patterns of ES-induced isometric contractions (e.g., 1.5-2.5 sec on-off duty cycle) of calf and thigh muscles could activate the skeletal muscle pump to significantly increase circulation, and reduce venous pooling. This was indicated by stroke volume and cardiac output increases (+12-30%) in able-bodied persons and those with SCI during rest in a sitting position. Several subsequent studies indeed confirmed that ES-induced muscle activation enhances peripheral and central circulatory responses, which alleviated venous pooling and excessive oedema in the legs, as well as orthostatic hypotension[45,46].

3. Increase of metabolism.

Third positive side effect of ES-induced muscle activation is that of a more active lifestyle and the increase of metabolism. Obesity is a serious problem in the general population nowadays, and even a bigger problem in the SCI population. People with an SCI have a lower rest metabolism caused by a lower muscle mass and a lower lean body mass, and even more often are completely (or partially) wheelchair bound as a result of their para- or tetraplegia. Studies have shown that the body mass index after SCI increases already during first months (during primary clinical rehabilitation), and significantly progresses after discharge. The percentage people with an SCI with obesity (BMI ≥ 22 kg/m2) significantly increased from 56% tot 75% in one-year time[47]. ES induced muscle activation might induce an increase of metabolism and reduce the risk of developing obesity in SCI[47].

4. Increase of (peripheral) nerve function

Another positive effect of ES might be the influence on the functioning of peripheral nerves. Although it is not likely that this induces increased feelings of well-being, it is worth mentioning in this paragraph. In a recent study, Lee et al. (2015) showed that intact (undamaged) nerves without signalling for example after SCI, decrease in function. According to Lee et al. there is accumulating evidence that peripheral motor axons deteriorate following SCI. This is reflected in compromised function, and shown in reduced compound muscle action potentials. Probably this effect is due to loss of optimal nerve guidance and not due to for example anatomic damage of myelin sheath. Clinical implications concern the acute phase and the future neuro-regenerative projects. Maintenance of peripheral nerves in the early phases of SCI may improve long-term rehabilitation outcomes. Evidence yet remains anecdotically[42].

5. Placebo effect.

Finally we like to address the possibility of ES-induced placebo effect. Not on objective findings like pressure or oxygenation, but on subjective findings from questionnaires. After an SCI the paralysed legs are inactive. Being able to activate the inactive paralysed muscles could generate (unconscious) confidence and faith in this (new) active therapeutic intervention. In general is known that the placebo effect more often is a powerful component of a treatment[56].

Methodological considerations

The randomised clinical trial in chapter three, and case series in chapters four to seven have several strengths. They especially give more insight in this newly developed method to apply ES to people with an SCI. Never before, as far as we know, ES has been applied in SCI, for a prolonged period of time, like 3 or 8 hours (respectively chapters four, five and seven), and have used specially designed ES-shorts.

Interface pressure measurements.

The relation between interface pressure and deep tissue deformation is interesting and has been studied before[48-53]. In order to study the effect of ES-induced muscle activation on (peak) pressure and pressure distribution, the interface sitting pressure was measured using a force-sensitive array (FSA, Vista Medical, Vancouver, Canada). In this thin 42 x 42cm soft flex mat 256 pressure sensors (1.82cm2 per sensor) have been incorporated. The mean IT pressure and pressure gradient were calculated.

The pressure gradient was calculated by subtracting the average of the 16 surrounding sensor values from the IT pressure. This pressure gradient may indicate shear forces and a high-pressure gradient is associated with high shear forces within the tissue, increasing the risk of developing PUs. Computerised models as in the studies of Breuls and Bouten (2003) give more insight, but are not for use in daily clinical practice[48-50]. In their studies was shown that skin interface pressure has a relation with deeper tissue damage, but duration of pressure,

tissue properties and blood flow through the tissue determine their relationship. Their computer model showed that highest stress concentrations due to interface pressure were found within deeper layers of the soft tissue. Although other studies on the relation between interface pressure and deep tissue injury are heterogeneous, the kind of correlation, linear or variable, remains disputable, all show a correlation between interface pressure and deep tissue deformity[48,49,50]. Therefore the conclusion can be that interface pressure measurements (although not absolutely) relatively represent deep tissue deformity.

Selection bias.
In our studies only Dutch persons with SCI between 18 and 66 with wheelchair dependency were included, eightyfive percent of them being men. Highly motivated, mostly because they had either been suffering from a PU in the past and wanted to do 'anything in their ability' to prevent a recurrence, or because they were eager to participate in any effect study as they mainly found that interesting to do, and 'it would not harm them'. The highly motivated participants might have been too positive, maybe too little critical as they were enthusiastic about the new concept. For example, the questionnaires may have been filled out too positive and may have caused a sampling bias. The representativeness of the results of the studies can nevertheless be generalised to the whole SCI population with an AIS classification A, B or C and an upper motor neuron lesion.

Small samples sizes.
In several studies we had to work with a relatively small number of participants. Nevertheless, statistical differences and effects were found. The smallest number of participants was in chapter seven (n= 8) in the two weeks overnight ES feasibility study. Differences and/ or effects might have been stronger when we had had larger groups to study. Maybe also effects or differences remained unsighted.

Implications for clinical practice

ES-induced activation of paralysed muscles could benefit PU care in SCI. The conceptual model shows how. I believe ES should be used more in rehabilitation settings. Activate those muscles! As stated in the general introduction to date, physicians are often not very familiar with ES treatment options, and prevention of PUs in clinical practice is generally more empirical, and seems not often based on evidence-based results. This might be a logical consequence of a 'vicious circle': ES is currently not often used for prevention of PUs and in protocols of scientific medical advisory boards it is not advised to do so, referring to a lack of evidence of efficacy. The clinical guidelines regarding the use of ES for PU management in SCI remain limited, and the lack of controlled studies is a serious problem, disallowing a definite statement on whether ES-induced exercise can actually prevent the incidence of PUs. In this perspective it is logical that health insurance companies do not (financially) support the use of ES as a standard

(preventive) treatment. This position raises a threshold for using ES in daily practice, seriously limiting frequent use, and feeds the unfamiliarity with applying ES. When a treatment is rather unknown in health care, the use will be critically and perhaps even skeptically reviewed. Consequently, ES in daily practice has become 'non-approachable', and is therefore currently not often used for prevention of PUs.

In clinical best practice it is not uncommon to prescribe therapies with no or very limited level of evidence. For example robot assisted treadmill therapy (e.g. 'Lokomat') is used frequently in rehabilitation treatment although the evidence is very limited and thin43. Therefore surprisingly ES is not used more often for PU prevention. Although controlled studies are still to be performed more, there are many effect studies proving positive effects of ES on risk factors for PU.

Costs of applying ES are low, compared to the high costs treatment of complications like PUs, it seems likely that the use of ES is cost effective. We have not found a study describing the cost effectiveness of ES. We therefore made a simple calculation ourselves in chapter 2.

Unfortunately, the method of activating muscles as in this study is not suitable for persons with a flaccid paresis like in cauda equina syndrome (lower motor neuron disease). Intact sensibility might also sometimes be a problem, as (transcutaneous) ES can be painful. In our studies though, four participants had incomplete lesions with partially intact sensibility (AIS B and C), but did not find the ES painful or even unpleasant. Activation of the muscle directly is also possible and is suitable for flaccid paralysis (lower motor unit, like cauda equina syndrome), but this is a different and alternative method and will not be disussed here in detail. It is likely that this ES-method in which the transcutaneous stimulus directly activates the muscle cells, without use of the spinal reflexes, leads to similar beneficial results as the method used in our studies.

Future perspectives

ES-induced muscle activation should be implemented in (medical) SCI rehabilitation programs in order to activate muscles and gain fitness and prevent complications like PUs. ES can be used for every person with an SCI during day and/ or overnight. In general, all persons with an SCI, and not a specially selected 'high risk group', are at risk for developing complications after a part of their body has got paralysed. The method used in our studies is usable for SCI with intact reflexes, an upper motor neuron lesion.

ES can be used in addition to the standard rehabilitation programs. People with an SCI need to continue to be trained in traditional rehabilitation programs, but in addition ES can be delivered during prolonged period of time during the day or overnight. For example, a person could continue to learn how to perform pressure relief movements in order to reduce continuous pressure loading of the buttocks, and also activate his paralysed leg muscles overnight while asleep (using ES).

Future research should firstly focus on ES-induced reduction of incidence of PUs. For preventing PUs it will be necessary to determine which reduction of pressure is clinically relevant and

therefore how often ES should be applied. The best method to gain more insight in the effects of ES on PU incidence is by conducting a longitudinal study with a control group. This could be a randomised clinical trial (RCT) comparing 2 groups of people with an SCI, with a follow-up period of 3-4 years. One group should take normal preventive measures in PU management, versus the other group taking the same preventive measures added with ES (-induced muscle contractions). Outcome measure could be PU incidence.

Methodological challenges to be addressed would be at first the inclusion of enough participants to make two comparable groups, secondly the high risk of dropouts in a follow-up of several years and, and thirdly (last but not least) the practical use of ES.

Second study focus could be on the effects of ES-induced muscle activation in increasing metabolism, reducing (over)weight. and obesity and a third interesting study should be in other patient groups than the SCI group, like for example paralysed patients on an intensive care unit. Maintenance of normal metabolism after a state of coma occurred might not only lead to less medical complications (like muscle atrophy and 'IC acquired weakness disease', but also to better functional outcome.

In order to make the application of transcutaneous ES as simple and effective as possible further research can reveal what protocol is optimal. Challenge is to find an optimal stimulation-rest interval in which muscles are optimally activated without too much muscle fatigue. This is very challenging as there are not only many different modes, but they are influencing each other as well (like frequency and pulse width). Fortunately there are adequate protocols already available.

To summarize, what new knowledge has been gained by this study?

This thesis answered several questions. They are summarised here:

Activation of both hamstrings and gluteal muscles of people with an SCI induces a larger interface pressure decrease while sitting than activation of gluteal muscles only. The ES protocol with an 'on-off' ratio of 1:4 seconds gives more interface pressure decrease in people with an SCI than with a 1:1 ratio, without marked muscle fatigue.

ES-induced muscle activation in people in a wheelchair is not as effective in reducing interface (sitting) pressure on the short term, as pressure relief movements (PRM's) (like bending forward) are. But the frequency of this muscle activation is so much higher that in the longer term it is much more likely to be effective in preventing PUs of the buttocks than PRM's. Moreover muscle activation has several other positive effects, like increase of muscle volume and increase of blood circulation. Paralysed muscles can be activated for a prolonged period of eight consecutive hours, under the condition that after 30 minutes of activation, there is a period of 30 minutes of rest. ES-induced muscle activation overnight (while lying in bed sleeping) using ES-shorts is a feasible method that does not disturb sleep. Using loose electrodes, or a specially designed ES garment are both methods to transcutaneously apply ES. Advantages of the ES garment over loose electrodes are that the electrodes do not have to be placed separately every time.

According to our participants the ES garment with electrical stimulator is feasible for daily use.

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9

Summary + Nederlandse samenvatting

Christof AJ Smit

Summary

Chapter 1, the general introduction, describes the background, the objective and the outline of the thesis. Approximately 2.5 million people worldwide live with a spinal cord injury (SCI). In the Netherlands approximately 12.500 people. SCI is a catastrophic event and causes the most drastic changes for an individual regarding physical status and lifestyle. Pressure ulcers (PUs) are the most prevalent secondary complication in individuals with an SCI, and of individuals admitted to a Model Systems facility within 24 hours of SCI 34% developed at least one PU during acute care or rehabilitation. The prevalence in chronic SCI is unacceptably high, throughout their lives, up to 85%. McKinley et al (1999), and others identified PUs as the most common secondary complication in all years after injury; and stated that an increased prevalence was associated with greater time since injury.

A PU is any lesion caused by unrelieved pressure resulting in damage of underlying tissue, involving the skin, fat, fascia, muscle, and bone. Therefore, unfortunately PUs are a common problem for wheelchair users such as individuals with an SCI, as they are constantly sitting, unable to stand or walk. When a PU occurs it often does at bony prominences such as the ischial tuberosities, the trochanters or sacal region. Treatment can either be conservative or operative and very often consists of mandatory bed rest to release pressure of the wound(s) and of surgery, leading to radical consequences such as decreased mobility and independence, delayed rehabilitation, and exclusion from work and social activities. This has a tremendous effect on the individual's physical and psychological condition. The consequences (of the treatment, and mining revenues), also result in high costs for the community.

Current PU preventive measures are insufficient. They are all extrinsic methods ('from outside the body'), trying to reduce pressure load, but unfortunately PUs still occur often. A problem with all the measures mentioned above is that they are passive measures that do not activate the muscles, which therefore do not ameliorate intrinsic risk factors ('from inside the body') for developing PUs such as muscle atrophy and decreased circulation. Electrical stimulation (ES) can induce paralysed muscle contractions and thus activate the muscle. It can, therefore, possibly be an active method to prevent these wounds.

Electrical stimulation (ES)- induced muscle activation may be a useful intervention that helps to prevent complications like PUs and allows immobilized individuals to remain seated or supine for prolonged periods of time, reducing the necessary frequency of assisted repositioning, and, most importantly, reducing the development of PUs. These periodically induced contractions may support or parallel the effects of passive methods like pressure-relief movements (voluntary or assisted repositioning), which are standard methods for PU prevention. The combination of intensity and duration of the pressure on soft tissue determines the total load and the deformity of the soft tissue. Tissue tolerance for deformity determines if the total load of pressure is harmful, causing a PU to occur or not. Tissue health and its tolerance for deformity therefore is important.

ES-induced muscle contractions could be helpful in increasing tissue health and its tolerance for deformity. ES-induced muscle contractions could theoretically reduce (interface) peak pressure, and improve intrinsic factors, like muscle volume and circulation. This could possibly be an active, instead of passive manner to reduce risk factors for developing PUs, and could be used in addition to the above-mentioned passive methods.

Physicians and therapists to date often seem not familiar with treatment options like ES. Both practical use of ES, and research in the field of PU prevention in SCI is difficult. There are limited scientific data available of each specific type of ES device. There are unanswered questions for example regarding the best ES protocol, optimal ES dose – response, what muscles to activate, and for how long before these muscles will stop contracting due to fatigue, and many more questions. Therefore, ES has long been a largely unknown and poorly understood modality. The prevention of PUs in clinical practice is not surprisingly generally empirical, and seems (logically) often based on dogma and rhetoric, rather than on evidence-based results. Objective of this thesis was to identify the updated evidence of effects of ES induced muscle activation and to investigate feasibility of a new PU prevention method. We used specially developed ES-shorts and evaluated different protocols of surface intermittent ES to gluteal and hamstrings muscles in wheelchair-bound people with an SCI, in an attempt to develop this method.

Chapter 2 gives a literature overview of the worldwide studies (between 1980 and 2014) that investigated effects of ES on risk factors for developing PUs in persons with an SCI. It shows that ES-induced exercise can have positive effects on factors reducing the risk of pressure sore development. Based on available data there is evidence that ES has positive influence on several risk factors for developing pressure ulcers (ischial tuberosities pressure, muscle volume, blood circulation, tissue oxygenation) in people with an SCI. However there is a lack of controlled studies, disallowing definite conclusions. It is hard to give a definite recommendation regarding the most adequate mode of ES, the optimal ES dose -response, training intensity, frequency or duration. There are indications nevertheless, and usable protocols. ES is safe and relatively simple to apply, and costs of applying ES are low. Results suggest that ES should be used more often in clinical practice and further study needs to be performed to study the relation between ES, risk factors for the development of PUs and PU prevention.

Chapter 3 presents a pilot study designed as a randomised clinical trial, in which we have studied the effects of surface ES of the gluteal muscles on the interface pressure. In thirteen participants with an SCI the gluteal muscles were activated using alternating and simultaneous surface electric stimulation protocols. Both stimulation protocols caused a significant decrease in interface pressure and pressure gradient during stimulation periods compared with rest periods. There was no significant difference in effects between the 2 protocols. We concluded that surface electric stimulation of the gluteal muscles in persons with SCI causes a decrease in interface pressure. This might restore blood flow in compressed tissue and help prevent pressure ulcers. We wondered whether positive effects on the interface pressure would increase if more and larger muscles were activated, besides the gluteal muscles only.

Therefore in chapter 4 case control series are presented that compare the effects of

electrically-induced activation of gluteal and hamstring muscles versus gluteal muscles only on sitting pressure distribution in individuals with an SCI. Furthermore the usability of the newly developed ES-shorts used, was evaluated. Ten participants underwent two electrical stimulation (ES) protocols applied using a custom-made electrode garment with built-in electrodes ('ES shorts'). In all participants, both protocols of gluteal and both gluteal and hamstrings ES-induced activation caused a significant decrease in IT pressure. IT pressure after both gluteal and hamstrings muscles activation was reduced significantly by 34.5% compared with rest pressure, whereas a significant reduction of 10.2% after activation of gluteal muscles only was found. The general usability of the ES-shorts was good, although there were some recommendations for improvement, like a solution for the ultrasound gel that came through the pockets during use, soiling the clothes.

In chapter 5 the effects of on-off two duty cycles (protocol 1:1 versus 1:4 sec.) are studied during 3 hours of ES-induced gluteal and hamstring activation on interface pressure distribution in ten sitting individuals with an SCI, and the usability of the newly, and further developed, ES-shorts were investigated again. In both protocols ES caused a significant decrease in average IT pressure compared to rest (or: no ES- induced muscle activation). On average 35% for protocol 1:4, and 13% for protocol 1:1. The ES on-off duty cycle 1:4s showed less muscle fatigue. Participants scored the usability of the ES-garment in general as satisfactory.

We found no extensive literature describing the effect of ES on ischial oxygenation. Therefore in a pre and post intervention cohort 12 participants performed pressure-relief movements (PRMs) (like bending forward while sitting in the wheelchair), and then after finishing the PRMs in succession received surface ES to the gluteal and hamstring muscles while sitting in their own wheelchair. Chapter 6 compares acute effects of ES-induced gluteal and hamstring muscle activation with pressure relief movements on interface pressure, blood flow and oxygenation. PRMs acutely reduced IP and improved oxygenation and BF in sitting wheelchair users with SCI. Although muscle activation also reduced IP, it may have been inadequate for all subjects to increase BF and oxygenation. The currently used method can therefore not replace the PRMs, but may be used additionally. Although acute effects may not be as good as those from PRMs, prolonged muscle activation may in contrast induce positive structural changes in muscle tissue, circulation, and pressure distribution.

In chapter 7 the feasibility of ES induced (paralysed) leg muscle activation was studied during prolonged overnight use. We studied muscle fatigue, sleep quality, and the usability of ES-shorts in people with an SCI when using overnight ES. The ES-shorts have not yet been tested for extended stimulation protocols, lasting longer than 3 hours, and only acute effects have been studied. Activating paralysed muscles overnight instead of during the daily routine prevents potential hinder of ES shorts in the wheelchair. We replaced the ultrasound gel for hydrofile graunules that also conducted well, but did not leave the pockets and gave no spots on the sheets. Furthermore some participants in our previous studies considered muscle activation at night as 'an ideal hassle free manner to prevent PU occurrence'. We activated the gluteal, hamstrings and quadriceps muscles in a 2-weeks overnight stimulation protocol,

8 hours per night, using specially developed ES-shorts. After 8 hours of activation muscles still contracted, although fatigue occurred and mean contraction size was lower at the end of the night (p=0.03). SQ-VAS (0-100) after intervention was 75, and 66 after 4 weeks without overnight ES (p=0.04) indicating ES improves sleep quality. The usability of the ES shorts was good. Therefore we concluded that overnight ES-induced muscle activation using ES-shorts in SCI is a new, feasible method that does not interfere with sleep.

The general discussion in chapter 8 reflects on the main findings and discusses the clinical implications. The study design and limitations of the study and future perspectives are considered. ES-induced muscle activation should be implicated in (medical) SCI rehabilitation programs in order to activate muscles and gain fitness and prevent complications like PUs. ES can be used for every person with an SCI during day and/ or overnight. In fact all persons are at risk for developing complications after a part of their body has got paralysed. The method used in our studies is usable for SCI (para- or tertaplegics) with intact reflexes, an upper motor neuron lesion. ES can be used in addition to the standard rehabilitation programs. People with an SCI need to continue to be trained in traditional rehabilitation programs, but in addition ES can be delivered during prolonged period of time during the day or overnight. For example, a person could continue to learn how to perform pressure relief movements (PRMs) in order to reduce continuous pressure loading of the buttocks, and also activate his paralysed leg muscles overnight while asleep (using ES).

Implications for clinical practice are the above ES-induced activation of paralysed muscles to be included in the SCI rehabilitation programs. Activate those muscles. There are sufficient reasons to advise to do this several moments per week a whole life long. Future research should firstly focus on ES induced reduction of incidence of PUs. For preventing PUs it will be necessary to determine which reduction of pressure is clinically relevant and therefore how often ES should be applied. The best method to gain more insight in the effects of ES on PU incidence is by conducting a longitudinal study with a control group. This could be a randomised clinical trial (RCT) comparing 2 groups of people with an SCI, with a follow-up period.

This thesis answered several questions. They are summarised here. Activation of both hamstrings and gluteal muscles of people with an SCI induces a larger interface pressure decrease while sitting than activation of gluteal muscles only. The ES protocol with an ‘on-off’ ratio of 1:4 seconds gives more interface pressure decrease in people with an SCI than with a 1:1 ratio, without marked muscle fatigue.

ES-induced muscle activation in people in a wheelchair is not as effective in reducing interface (sitting) pressure on the short term, as pressure relief movements (PRM’s) (like bending forward) are. But the frequency of this muscle activation is so much higher that in the longer term it is much more likely to be effective in preventing PUs of the buttocks than PRM’s. Moreover muscle activation has several other positive effects, like increase of muscle volume and increase of blood circulation. Paralysed muscles can be activated for a prolonged period of eight consecutive hours, under the condition that after 30 minutes of activation, there is a period of 30 minutes of rest. ES-induced muscle activation overnight (while lying

in bed sleeping) using ES-shorts is a feasible method that does not disturb sleep. Using loose electrodes, or a specially designed ES garment are both methods to transcutaneously apply ES. A big advantage of the ES garment over loose electrodes is that the electrodes do not have to be placed separately every time. According to our participants the ES garment with electrical stimulator is feasible for daily use.

Samenvatting (Summary in Dutch)

Hoofdstuk 1, de algemene inleiding beschrijft de achtergrond, het doel en de opzet van de studies van dit project. Er leven op de wereld ongeveer 2,5 miljoen mensen met een dwarslaesie. In Nederland zijn dat er ongeveer 12.500. Als iemand een dwarslaesie krijgt is dat vreselijk en verandert het leven voor die persoon dramatisch op zowel fysiek, mentaal als op sociaal-maatschappelijk vlak. Decubitus is de daarbij meest voorkomende secundaire complicatie. De prevalentie tijdens zowel de acute zorg of revalidatie, als in de chronische fase is onaanvaardbaar hoog. Er zijn studies die beschrijven dat 85% van de mensen met een dwarslaesie gedurende het leven decubitus krijgen. McKinley et al (1999), heeft bovendien aangetoond dat de prevalentie toeneemt met het verstrijken van de tijd na het krijgen van de dwarslaesie ('de leeftijd van de dwarslaesie').

Decubitus is een wond veroorzaakt door druk- en schuifkrachten, met schade aan de huid, vet, fascie, spieren en vaak ook bot. Rolstoelgebruikers zoals mensen met een dwarslaesie, hebben een verhoogd risico op het krijgen van zo'n wond omdat ze voortdurend zitten, en niet in staat zijn om (even) op te staan of een stuk te lopen. Decubitus onstaat meestal in het weefsel op benige uitsteeksels zoals de tubera ischiadica (zitbeenknobbels), de trochanters van de femurs, of het sacrum. De behandeling van deze wonden kan zowel conservatief of operatief zijn, en bestaat bijna altijd uit verplichte bedrust om de druk van de wond(en) te ontlasten. Dit heeft begrijpelijk een enorme invloed op de individuele fysieke en psychische conditie, en daarnaast ingrijpende gevolgen voor het zelfstandig functioneren. Denk aan de gevolgen als de verminderde mobiliteit en afhankelijkheid in de persoonlijke verzorging, de vertraagde revalidatie, en niet alleen uitsluiting van het werk en sociale activiteiten, maar ook het lang niet thuis in het gezin kunnen zijn. Deze gevolgen en de behandeling ervan leidt bovendien tot hoge kosten in de gezondheidszorg en dus voor de gemeenschap.

De huidige preventieve maatregelen blijken ontoereikend, want decubitus komt nog veel voor. Goede zitkussens, op maat gemaakte rolstoelen, drukontlastende bewegingen en meer: het zijn allemaal preventieve, maar extrinsieke methoden (van buiten het lichaam), met als doel het reduceren van zitdruk en verminderen van schuifkrachten. Het probleem hiervan is dat het passieve maatregelen zijn, die de spieren niet activeren, en dus geen verbetering van intrinsieke risicofactoren (van binnen in het lichaam) geven. Denk hierbij aan bijvoorbeeld spieratrofie en verminderde bloedcirculatie. Elektrische stimulatie (ES) kan verlamde spieren activeren, als het ware de functie van het centrale zenuwstelsel over nemen en zo een actieve methode zijn om deze wonden te voorkomen. Deze geïnduceerde spiercontracties kunnen uiteraard gegeven worden naast, en aanvullend op de andere (passieve) preventieve maatregelen om decubitus te voorkomen. Niet in plaats van dus.

De combinatie van de intensiteit en duur van de druk op de weke delen bepaalt de totale belasting en de vervorming ervan. Weefseltolerantie voor vervorming bepaalt of de totale belasting tot schade leidt, en er decubitus ontstaat. De gezondheid van het weefsel en de tolerantie voor vervorming is daarom belangrijk. ES-geïnduceerde spiercontracties kunnen

helpen om de gezondheid van weefsel en de tolerantie voor misvorming te vergroten. ES-geïnduceerde spiercontracties kunnen theoretisch de piekdruk op de tubera ischiadica verminderen, en intrinsieke factoren zoals spiervolume en de bloedcirculatie verbeteren.
Artsen en therapeuten lijken vaak niet vertrouwd met de behandeloptie van elektrostimulatie. Er is een soort drempel voor praktisch gebruik van ervan bij mensen met een dwarslaesie. Het wetenschappelijk onderzoek op het gebied van decubituspreventie bij dwarslaesie is moeilijk. Wetenschappelijke gegevens over het gebruik van elk specifiek type ES-apparaat zijn er nauwelijks of niet. Er zijn onbeantwoorde vragen bijvoorbeeld met betrekking tot de beste ES protocol, optimale ES dosis - response, welke spieren te activeren, en hoe lang voordat deze spieren te vermoeid raken, en nog veel meer vragen. Daarom is ES een relatief onbekend (en dus ook 'onbeminde') behandelmethode. De behandeling en preventie van decubitus in de klinische praktijk is niet verrassend, het algemeen empirisch, en lijkt (logisch) vaak gebaseerd op dogma's en retoriek, 'dit doen we altijd zo…', in plaats van op evidence-based resultaten. Niet per se verkeerd overigens, maar het doel van dit proefschrift was om de bijgewerkte bewijs van de effecten van ES geïnduceerde spieractivatie te identificeren en om de haalbaarheid van een nieuwe decubituspreventiemethode te onderzoeken. We hebben speciaal voor het onderzoek Elektrostimulatie broeken, 'ES-shorts' laten maken (Firma Axiobionics in Michigan, Verenigde Staten van Amerika). Deze ES broek heeft ingebouwde elektroden, die automatisch contact maken met de huid. Wel moet er een hydrofiele gel of hydrofiele korrels in kleine zakjes worden aangebracht voor de optimale geleiding van de elektrische puls tussen de elektroden en de huid. Met deze ES broek zijn verscheidene protocollen van spieractivatie van de bilspieren en de hamstrings getest bij rolstoelgebonden mensen met een dwarslaesie, met als doel te komen tot een bruikbare methode om elektrostimulatie toe te passen.
Hoofdstuk 2 is een literatuuroverzicht van de wereldwijde studies tussen 1980 en 2014, die effecten van ES hebben beschreven op risicofactoren voor het ontwikkelen van decubitus bij dwarslaesie. Beschreven worden de effecten van ES-geïnduceerde spiercontracties op de factoren die de kans op decubitus beïnvloeden. Op basis van de beschikbare gegevens zijn er aanwijzingen dat ES heeft een positieve invloed heeft op een aantal risicofactoren. Denk aan: druk op de zitbeenknobbels, spiermassa, bloedsomloop, weefseloxygenatie bij mensen met een dwarslaesie. Er is een gebrek aan grote en gecontroleerde studies, waardoor definitieve conclusies niet kunnen worden getrokken. Het is moeilijk om een definitieve advies over de meest geschikte wijze van ES, de optimale dosis en respons ES, training intensiteit, frequentie of duur te geven. Er zijn desalniettemin duidelijke aanwijzingen dat ES geïnduceerde spiercontracties gunstige invloed hebben op de risicofactoren voor decubitus, en er zijn bruikbare protocollen voor de dagelijkse praktijk. ES is veilig en relatief eenvoudig aan te brengen, en de kosten voor het toepassen van ES zijn laag. De resultaten suggereren dat ES vaker zou moeten worden gebruikt in de klinische praktijk. Verder onderzoek moet zich richten op het verlagen van de incidentie van decubitus.
In Hoofdstuk 3 wordt een pilotstudie beschreven. In een gerandomiseerde klinische trial, zijn bij dertien deelnemers met een dwarslaesie de effecten van transcutane ES van de bilspieren

op de zitdruk bestudeerd. Afwisselend werden de linker en rechter bilspieren geactiveerd met transcutane elektrostimulatie. Van twee stimulatieprotocollen gaven beide een significante daling van de zitdruk en zitdrukgradiënt tijdens de stimulatie vergeleken met rustperiodes. Wij concludeerden derhalve dat dat activatie van alleen de bilspieren middels ES bij mensen met een dwarslaesie een (acute) verlaging van zitdruk geeft. Dit kan helpen bij het herstellen van de bloedstroom in gecomprimeerd weefsel en dus ook bijdragen aan preventie van decubitus. We vroegen ons af of de positieve effecten op de zitdruk zouden toenemen als er naast alleen de bilspieren meer en grotere spieren werden geactiveerd.

Daarom wordt in hoofdstuk 4 een case-control-serie gepresenteerd, waarin de drukverdeling door activatie van de bilspieren en hamstrings versus bilspieren alleen worden vergeleken (bij mensen met een dwarslaesie). Ook werd de bruikbaarheid van de nieuw ontwikkelde ES-shorts bevraagd middels een enquête. Tien deelnemers ondergingen elk twee stimulatieprotocollen met een op maat gemaakte (korte) broek met ingebouwde elektroden. Bij alle deelnemers gaven beide protocollen van zowel (alleen) de beide bilspieren als ook beide bilspieren en hamstrings een significante daling van de zitdruk. Activatie van zowel bilspieren als hamstrings was echter significant effectiever met 34,5% ten opzichte van rust, terwijl activatie van alleen de bilspieren een (significante) drukverlaging gaf van 10,2%. De bruikbaarheid van de ES-shorts was goed, waarbij er enkele aanbevelingen werden gegeven voor verbetering. Bijvoorbeeld een oplossing voor het lekken van de de ultrasone gel, die tijdens het gebruik door de zakken kwam in de kleding.

In hoofdstuk 5 werden de effecten van twee stimulatieprotocollen met elkaar vergeleken. Het verschil tussen de protocollen was de tijd waarin de spieren niet geactiveerd werden, cq. de rustperiode. Het eerste protocol bestond uit 1 seconde speiractivatie, ‘aan’, vervolgens 1 seconde rust, cq. geen spieractivatie of ‘uit’, versus protocol twee: 1 seconde aan met 4 sec uit. Dit gedurende een periode van drie uur achtereen, waarbij de deelnemers de ES broek droegen in hun eigen rolstoel. Uitkomstmaten waren de zitdrukverdeling, en de gebruikersvriendelijkheid van de (nieuwe verder ontwikkelde) ES broek. In beide protocollen veroorzaakte ES een significante daling van de gemiddelde zitdruk onder de tubera ischiadica in vergelijking met rust (of: geen ES-geïnduceerde spier activering). Gemiddeld 35% bij protocol 1: 4, en 13% van protocol 1: 1. Bij het 1:4s protocol bleven de spieren tot het laatst goed activeerbaar, waarschijnlijk omdat ze minder vermoeid waren dan bij het 1:1 protocol. De deelnemers scoorde de bruikbaarheid van de ES-broek in het algemeen als ruim voldoende.

Hoofdstuk 6 vergelijkt acute effecten van ES-geïnduceerde gluteus- en hamstringsactivatie met drukontlastende bewegingen. Denk hierbij aan sterk naar voren buigen zittend in de rolstoel, of sterk naar een zijde. Uitkomstmaten waren de zitdruk, de doorbloeding en zuurstoftoevoer van de het zitvlak ter hoogte van de tubera ischiadica. In de literatuur hebben we slechts weinig literatuur gevonden, waarin het effect van ES op de oxygenatie van het zitvlak wordt beschreven. De studie hebben we opgezet als een pre- en post interventie cohortstudie, bestaande uit 12 personen met een dwarslaesie in hun eigen rolstoel. Zitdruk, doorbloeding en oxygenatie van het zitvlak werd eerst gemeten tijdens drukontlastende bewegingen, en vervolgens tijdens

spieractivatie van gluteaal en hamstringspieren. Drukontlastende bewegingen verminderden de zitdruk (acuut), en verbeterden zowel de doorbloeding als de oxygenatie. Bij spieractivatie verminderde ook de zitdruk en de verbeterde de piek doorbloeding, echter niet de gemiddelde doorbloeding noch de oxygenatie. De gebruikte methode van spieractivatie kan dus niet in plaats van drukontlastende bewegingen worden gebruikt, maar natuurlijk wel aanvullend. Want hoewel de acute effecten niet zo goed als die van drukontlasting van het zitvlak kan langdurige spieractiviteit positieve structurele veranderingen geven van het spierweefsel, de circulatie, oxygenatie en drukverdeling.
In hoofdstuk 7 werd de haalbaarheid ('feasibilty') van ES geïnduceerde beenspieractivatie onderzocht bij langdurig gebruik 's nachts. We bestudeerden spiervermoeidheid, kwaliteit van de slaap, en de bruikbaarheid van de ES-broek bij mensen met een dwarslaesie. De ES broek hadden we nog niet getest gedurende een langere periode dan 3 uur, en daarbij alleen acute effecten onderzocht. Daarbij zou gebruik gedurende de nacht een aantal voordelen kunnen opleveren ten opzichte van gebruik overdag. Bijvoorbeeld elke mogelijke vorm van hinder in de rolstoel . Enkele deelnemers in onze vorige studies beschouwden bovendien nachtelijke spieractivatie als 'een ideale methode om decubitus te voorkomen'. We hebben bij 8 mensen gedurende twee weken, 8 uur per nacht de bilspieren, hamstrings en quadriceps geactiveerd. Hiervoor hebben we een Es-broek gebruikt die speciaal geschikt is voor gebruik in bed. Het stimulatieprotocol bestond uit een half uur activatie volgens het eerder geteste 1:4 protocol, gevolgd door een half rust. Resultaten lieten zien dat met dit protocol na 8 uur de spieren nog samentrokken, hoewel vermoeidheid opgetreden was, want de gemiddelde sterkte van de contracties aan het einde van de nacht bleek significant lager was dan aan het begin. De slaapkwaliteit verbeterde met ES. Op de scorelijst voor ervaren slaapkwaliteit (de zogenaamde SQ-VAS) (0-100) gaven de deelnemers hun slaap met ES 75 punten en zonder 66 op een schaal van 0-100 punten (statistisch significant). De bruikbaarheid van de ES-broek met stimulator werd beordeeld als ruim voldoende tot goed. Conclusie van deze studie was derhalve dat nachtelijke ES- geïnduceerde spieractivatie met behulp van een speciale ES-broek een nieuwe, haalbare methode is, die bovendien de slaap niet verstoord.

De algemene discussie in hoofdstuk 8 reflecteert op de belangrijkste bevindingen en bespreekt de klinische implicaties van de studies in dit boek. Ook worden hierin de onderzoeksopzet en de beperkingen van het onderzoek, evenals toekomstperspectieven beschreven. ES-geïnduceerde spieractivatie zou geïmplementeerd moeten worden in de dwarslaesierevalidatie programma's om middels spieractivatie verlamde spieren min of meer gezond te houden en complicaties als decubitus te voorkomen. Hiervoor kan elektrostimulatie zowel overdag als 's nachts worden gebruikt. In feite hebben alle mensen met een dwarslaesie in een rolstoel een verhoogd risico op het ontwikkelen van complicaties. De methode die wordt gebruikt in onze studies is bruikbaar voor mensen met een dwarslaesie met intacte spinale reflexen, dus met een zogenaamde 'upper motor neuron' laesie. Spieractivatie met ES kan worden gebruikt als aanvulling op de standaard revalidatie programma's, met name aanvullend op

zogenaamde (anti)decubitusmodules. Met andere woorden: het is belangrijk dat mensen met een dwarslaesie leren maatregelen te nemen om decubitus te voorkomen. Om bijvoorbeeld drukverlagende bewegingen uit te voeren om de continue drukbelasting van het zitvlak te verminderen, en daarbij ook zijn verlamde beenspieren te activeren, bijvoorbeeld 's nachts tijdens de slaap.

Implicaties voor de klinische praktijk: de bovenstaande ES-geïnduceerde activatie van verlamde spieren moet standaard worden toegepast in het dwarslaesie revalidatie behandelprogramma. Activeer die spieren! Er zijn voldoende redenen om te adviseren om dit op meerdere momenten per week een heel leven lang te doen. Toekomstig onderzoek moet zich in de eerste plaats richten op incidentie van decubitus. Het is nodig om te bepalen welke drukafname klinisch relevant is en hoe vaak ES moet worden toegepast om decubitus te voorkomen. De beste methode om dit de doen is middels een incidentiestudie bij twee groepen mensen met een dwarslaesie, waarbij middels vergelijkend onderzoek in een gerandomiseerde klinische trial (‘randomised clinical trial’) het effect van spieractivatie op de incidentie van decubitus wordt onderzocht.

Dit proefschrift beantwoordt een aantal vragen, die hier worden samengevat: activatie van zowel de hamstrings en bilspieren van mensen met een dwarslaesie geeft een grotere zitdrukverlaging dan de activering van alleen de bilspieren. Het ES-protocol met een ‘aan-uit’ verhouding van 1: 4 seconden geeft meer zitdrukafname bij mensen met een dwarslaesie, dan met een 1: 1 verhouding, zonder duidelijke spiervermoeidheid. ES-geïnduceerde spieractivatie bij mensen in een rolstoel is niet zo effectief in het verlagen van zitdruk op de korte termijn, als drukverlagende bewegingen (zoals bijvoorbeeld naar voren buigen). De frequentie echter van deze spieractivatie is zoveel hoger, dat dit op langere termijn waarschijnlijk effectiever is in het voorkomen van decubitus. Bovendien geeft spieractivatie een aantal andere positieve effecten, zoals toename van spiermassa en een toename van de bloedcirculatie. Verlamde spieren kunnen gedurende een langere periode van acht opeenvolgende uren worden geactiveerd, onder de voorwaarde dat na 30 minuten van activatie, er een periode van 30 minuten rust volgt. Spieractivatie gedurende de nacht, slapend liggend in bed, met een ES-broek is goed mogelijk zonder dat het de slaap verstoord. Het is overigens zowel mogelijk om ES toe te passen door de ES broek te gebruiken of door lossen electroden te gebruiken. Beide methoden hebben voor- en nadelen. Voordeel van de ES–broek ten opzichte van losse elektroden is dat de elektroden niet steeds afzonderlijk op de huid moeten worden geplakt. Volgens de deelnemers is de ES-broek met de gebruikte elektrische stimulator ruim voldoende gebruikersvriendelijk voor dagelijks gebruik.

10

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Christof AJ Smit

Dankwoord

Heel fijn dat dit nu klaar is. De kaft zit er omheen. Promoveren is vooral doorzetten. In mijn geval tegen doorzitten. Het muurtegeltje op het Duyvens Nagel Onderzoekslaboratorium in Reade: 'Als het makkelijk was kon iedereen het', heeft me geregeld geprikkeld om door te gaan.

Ik ben 'onderzoek doen' leuk gaan vinden de afgelopen jaren. Dat heeft vooral te maken met mijn motivatie om decubitus bij mensen met een dwarslaesie de wereld uit te helpen. Als mensen een dwarslaesie krijgen maken ze een persoonlijke ramp door. Ik vind het als revalidatiearts op een dwarslaesieafdeling van een revalidatiecentrum mooi en dankbaar om ze samen met een gemotiveerd team te revalideren. Hoofddoel van de revalidatie is dat mensen hun leven weer kunnen oppakken, fit blijven en complicaties voorkomen. Dat lukt ze. Nooit vanzelf, maar altijd met ups en downs en heel hard werken. Vaak heb ik gehoord dat het leven na een dwarslaesie heel anders is dan ervoor, en weliswaar meestal in een rolstoel, maar uiteindelijk wel weer met kwaliteit. Die gaat echter verloren, als er decubitus ontstaat. Een (grote) wond, vaak op het zitvlak, die vaak alleen geneest met liggen of met een operatie, en die mensen uit hun maatschappelijke en privéleven rukt. Dat drijft mensen tot wanhoop. Die maak ik op de wondpoli en op de afdeling wekelijks mee in mijn werk. Acht jaar geleden ben ik aan dit onderzoeksproject begonnen omdat ik aan deze wanhoop iets wilde doen. Nu is het begin er, dit stuk is klaar. De uitkomsten van dit onderzoek dragen bij aan de preventie van decubitus. Ik ben er trots op dat Reade elektrostimulatie heeft ingepast in het behandelprogramma en dat er een wetenschappelijk vervolg is op deze studies, onder andere in de samenwerking met onderzoekers van de universiteit van Liverpool en het Reavalidatiecentrum Stoke Mandeville in Engeland.

Deze promotie was me niet gelukt zonder hulp van veel mensen. Mensen die zich hebben ingezet bij het onderzoek, mensen die werken in Reade, waarmee ik samenwerk in de praktijk, maar ook familie en vrienden, en mensen die zich juist niet zo met mijn onderzoek bezig waren, maar waar ik wel extra energie en inspiratie van kreeg. Die wil ik graag allemaal bedanken en een aantal wil ik bij naam noemen.

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Beste Janneke, fijne collega uit de kliniek, co-promotor. Wij delen onze interesse voor de dwarslaesierevalidatie. Tot april 2013 werkten we samen in Reade, wat ik prettig vond. Jouw grappen waren soms nog slechter dan de mijne. Dus we hebben veel gelachen samen. Als collega was je voor mij betrouwbaar en ondersteunend. Jij begreep van iedereen natuurlijk het beste hoe moeilijk het soms is, om naast je klinische werk bezig te zijn met onderzoek, en hebt me onder andere meermaals aangespoord om een schrijfweek in te plannen. Jij nam dan voor me waar in de kliniek. Je adviezen waren en zijn altijd waardevol en praktisch. Dank je wel. Heel fijn dat je weer terug bent in het Nederlands Vlaams Dwarslaesie Genootschap (NVDG).

Toen ik aan dit project begon, wilde ik niet dat mijn gezin daaronder zou moeten lijden, of ik zelf overspannen zou raken. Ik heb daarom tijd gevraagd en gekregen van de Raad van Bestuur van Reade en daarna van mijn collega's in de medische staf (van toen nog het Revalidatiecentrum Amsterdam). Jos Buijs, wijlen Peter Koppe (overleden 23 juni 2012) en Mattie Schinkel: jullie stonden vanaf het begin positief tegenover mijn onderzoek. Dank voor jullie belangstelling en waardevolle ondersteuning in tijd. Inmiddels is Anne Marie ter Steeg in 2014 als medisch manager aangesteld. In deze roerige tijd, met bezuinigingen, ervaar ik onze samenwerking als open en constructief. Het expertisecentrum Elektrostimuatie in Reade is een feit!

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Collega's van het Nederlands Vlaams Dwarslaesie Genootschap (NVDG). De hele groep!
Ik waardeer ons open en eerlijke, directe contact. Ik ervaar een goede combinatie van vakinhoudelijke verdieping, serieuze overleggen en gezelligheid. Samen naar het ISCoS. Mijns inziens is de kracht van het NVDG het delen van kennis en het samenwerken. Laten we gezamenlijk de kwaliteit van de dwarslaesierevalidatie in Nederland en Vlaanderen blijven bewaken, juist nu in tijden van bezuinigingen.

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Promovendi die pas na het afronden van hun proefschrift weer tijd hebben voor hun gezin, hebben mijn inziens een verkeerde keuze gemaakt. Door het afronden van dit project is er echter wel weer wat meer ruimte in mijn hoofd en dat helpt wel thuis wat leuker aanwezig te zijn. Lieve, lieve Adje, jij bent 'met name goed in alles' en ik ben erg blij met jouw onvoorwaardelijke steun en onze sterke verbondenheid. Elke dag weer ben ik blij dat ik jou ooit op de Kroeg ben tegengekomen.
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Tot slot zou ik nog willen stellen dat:

1. Veel mensen met een dwarslaesie vertellen dat niet meer kunnen lopen, lang niet het ergste is van alle problemen. Dat zijn vooral de terugkerende complicaties. Zo krijgt 85 % van de mensen met een dwarslaesie gedurende het leven te maken met decubitus.

2. Activatie van zowel de hamstrings als de bil ('gluteaal') musculatuur van mensen met een dwarslaesie meer drukverlaging geeft van de druk op de zitvlak (rond de zitbeenderen), dan activatie van alleen de gluteaal musculatuur.

3. Elektrostimulatie met een 'aan-uit' verhouding van 1:4 meer drukverlaging geeft dan met de verhouding 1:1 gedurende een stimulatie periode van 3 uur, zonder te veel spiervermoeidheid.

4. Het aforisme 'La médecine c'est guérir parfois, soulager souvent, consoler toujours' [geneeskunde is er om soms te genezen, vaak te verlichten, en altijd te troosten] van de Franse chirurg Ambroise Paré (1510-1590), in sterke mate geldt voor de dwarslaesierevalidatie.

5. Voor mensen in een rolstoel spieractivatie middels elektrostimulatie niet zo effectief is als bijvoorbeeld vooroverbuigen om druk op/ rond de zitbeenderen te verlagen, maar de frequentie van deze spieractivatie zo veel hoger ligt dat daarmee spieractivatie op de lange duur waarschijnlijk wel effectiever is, dan bijvoorbeeld vooroverbuigen in het voorkomen van drukwonden.

6. Verlamde spieren 8 uur lang geactiveerd kunnen worden, mits er in een uur na 30 minuten activatie vervolgens 30 minuten rust gegeven wordt.

7. Nachtelijke spieractivatie middels een elektrostimulatie broek, een methode is die goed wordt verdragen en de slaap niet verstoord, integendeel.

8. Promovendi die pas na het afronden van hun proefschrift weer tijd hebben voor hun gezin, mijn inziens een verkeerde keuze hebben gemaakt.

9. Promoveren is vooral doorzetten. In mijn geval tegen doorzitten. Het muurtegeltje op het Duyvens Nagel Onderzoekslaboratorium in Reade: 'Als het makkelijk was kon iedereen het', heeft me regelmatig geprikkeld om door te gaan.

10. Het is voor mensen zonder dwarslaesie goed om te weten dat als je elektrostimulatie niet kunt verdragen, wielrennen een goed alternatief is. Het geeft fysieke en mentale gezondheid, want na het fietsen is de bloeddruk lager en het hoofd altijd weer leeg.

About the author

Christof AJ Smit [46] was born in Tilburg on the 16 th of june **1970**. He finished his secondary school (Gymnasium β) in Sittard in **1988**.

In **1996** he finished the (pre- and) clinical part of the medical school at the University of Nijmegen ('artsexamen'), and received his docters degree (MD).

He worked at accidents and emergencies ('spoedeisende hulp') in Oss for 1 year. Then he went to Wigan (United Kingdom) to work as a senior house officer ('zaalarts') in orthopedics and trauma.

In **1998** he started his traineeship to become a Rehabilitation physician, in Rehabilitation center 'Heliomare' (Wijk aan Zee), and the VU medical center in Amsterdam. He successfully finished this traineeship in 2002.

From **2002** until today he works as a physician in 'Reade', Center for Rehabilitation and Rheumatology in Amsterdam (previously: 'Rehabilitation Center Amsterdam'), and is specialized in spinal cord injury rehabilitation. From 2013, he is one of the two trainers for the medical specialization of Rehabilitation Medicine for residants, in co-operation with the educational institutes connected to the two academic medical hospitals in Amsterdam (Academic Medical Center and VU Medical Center, the Netherlands).

In **2008** Christof started his PhD study besides his work as a (rehabilitation) physician in Reade.

He is married to Adje Smit-Giesen and has got four sons: Oscar [13], Christof [12], Lucas [11] and Duco [10 years old]. They live in Abcoude, near Amsterdam.

List of Publications

Journal Publications

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